PROCEEDINGS

Workshop

on the draft

Regulations

for

Biotechnology Products

under the

Canadian Environmental Protection Act

Environment Canada Health and Welfare Canada

Ottawa, January 21-22, 1991

WORKSHOP ON THE DRAFT REGULATIONS FOR BIOTECHNOLOGY PRODUCTS UNDER THE CANADIAN ENVIRONMENTAL PROTECTION ACT

A Workshop, as part of the consultative process to develop regulations for the notification of biotechnological products under the Canadian Environmental Protection Act.

21-22 January, 1991
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FOREWORD

Environment Canada and Health and Welfare Canada held this workshop recognizing that consultation with the public is an integral part of the regulatory process. This workshop provided a forum, as part of the consultative process, initiated in 1990, to develop regulations for the notification of new biotechnology products under the **Canadian Environmental Protection Act** (**CEPA**), to safeguard public health and protect the environment. The development of the information requirements will benefit from the contributions made by the participants and from the interchange of different points of view, concepts, and concerns.

This Proceedings presents the position papers from various sectors which provided the background and focus for the discussions. Also included is the dialogue of the participants of the workshop relating to the substances that will be regulated under CEPA, and to the regulations and guidelines that are still under development; a successful dialogue that resulted in many well-reasoned recommendations, clarified many concerns of participating sectors, and provided a useful platform for future discourse.

Background documents provided to participants can be found in Appendices I and II.

EDITOR'S NOTE

The discussions presented in the Proceedings were transcribed from audio tapes recorded during the workshop. Instances occur where the quality of the recording, or non-recorded gaps, made transcription a matter of conjecture.

It has not been possible to contact all participants to allow them to edit their contributions, so some editorial license has been invoked. In the same vein, not all lead speakers submitted hard-copies of their talks. In these instances it has been necessary to transcribe their papers and present them in these Proceedings without benefit of some of the accompanying projected material or, in other cases, the speakers, notes.

Finally, the views expressed by the participants should not necessarily be construed as the official positions of their parent organizations.

Ian L. Stevenson Ed.

WORKSHOP ON THE DRAFT REGULATIONS FOR BIOTECHNOLOGY PRODUCTS UNDER *the CANADIAN ENVIRONMENTAL PROTECTION ACT (CEPA)*

PROGRAM

Monday, January 21, 1991

8:00 Registration

PLENARY SESSION

Location: Theatre

Chair: **Dr. Keith Bailey**, Director, Bureau of Drug Research, Drugs Directorate, Health and Welfare Canada.

8:45-9:00 CEPA, An Introduction to the Regulations.
Dr. John A. Buccini, Director, Commercial Chemicals Branch, Environment Canada.

9:00-9:30 The Development of CEPA Biotechnology Regulations.
Dr. Terry McIntyre, Biotechnology Section, Commercial Chemicals Branch, Environment Canada.

The Role of Health and Welfare Canada in CEPA.
Dr. John Smith, Biotechnology Section, Environmental Health Directorate, Health and Welfare Canada.

9:30-10:00 An Academic Perspective on the Proposed CEPA Regulations.
Dr. Campbell Wyndham, Carleton University, Ottawa.

10:00-10:30 **COFFEE**

10:30-11:00 The US-EPA Perspective on Biotechnology.
Dr. Larry Zeph, Office of Toxic Substances,
United States Environmental Protection Agency, Washington, D.C.

11:00-11:30 An Environmentalist's Perspective.
Paul Muldoon, Canadian Institute for Environmental Law and Policy, and Pollution Probe, Toronto.

11:30-12:00 An Industrial Perspective.
Rob Quinn, President, Industrial Biotechnology Association of Canada, Ottawa.

12:00-12:15 Discussion

12:15-12:30 Tasking of Syndicates. **Dr. Sheila Forsyth,** Biotechnology Section, Commercial Chemicals Branch, Environment Canada.

12:30-13:30 **LUNCH**

13:30-16:30 **SYNDICATES**

Tuesday, January 22, 1991

8:30-9:00 Plenary session/Theatre - Progress in syndicates. **Dr. Sheila Forsyth**

9:00-12:00 **SYNDICATES** (Coffee will be provided in the syndicate rooms.)

12:00-13:30 **LUNCH**

13:30-14:45 Plenary, **SYNDICATE REPORTS**, Chair: **Rob Quinn.**

14:45-15:15 **COFFEE**

15:15-16:30 **SYNDICATE REPORTS,** Discussion and Wrap Up

PLENARY SESSIONS

OPENING REMARKS

Dr. Keith Bailey
Director, Bureau of Drug Research
Drugs Directorate
Health Protection Branch
Health and Welfare Canada

Good morning, ladies and gentlemen. Welcome on behalf of the regulatory departments involved in the drafting of the CEPA regulations. I suspect the reason I've been asked to host this session is because I have chaired the biotechnology committee of the Health Protection Branch of Health and Welfare Canada for the past three or four years. I will shortly take over the chair of the Interdepartmental Working Group on the Safety and Regulations in Biotechnology. The chair of this latter group is rotated among the principal departments involved in regulations in biotech -- that is, Agriculture Canada, Environment Canada, and Health and Welfare Canada.

In December last year the federal government published one of its backgrounder papers on its regulatory reform initiatives which I would like to quote to you.

The objectives of the initiatives:

- to provide a better opportunity for public participation in the regulatory process
- to place the accountability and responsibility for regulatory decisions back in the hands of Ministers, and
- to ensure that greater precision and discipline are brought to bear on the regulatory process.

The foundation of the regulatory reform strategy is a process that not only encourages an open dialogue with those affected by proposed regulations, but also places a burden on the government to take account of their concerns.

The main elements of the process are:

- accountability - more and better information is now required, particularly in regard to the outcome of public consultations before proposed regulations will be considered for either pre-publication (Canada Gazette Part I) or for final approval (Canada Gazette Part II).

These changes have resulted in a shift away from attempts to achieve economic objectives by using regulations as a substitute for market discipline. The regulatory reform strategy has allowed greater emphasis to be placed on areas such as health, safety, and protection of the environment, where alternatives to an effective regulatory framework are not practical.

Public participation has been a key feature of the regulatory reform strategy that helped bring about these improvements. Regulation making must continue to be a truly joint venture between the government and the public if Canada is to maintain an effective regulatory framework.

So we are here this morning as part of this important process. We are grateful to Environment Canada and Health and Welfare Canada principally who have been busy organizing this workshop. The first part of the program will consist of a number of plenary speakers representing many of the interest groups who are here. We will hear from the United States Environmental Protection Agency, who have been going through much the same process as is occurring in the development of these regulations under the Canadian Environmental Protection Act (CEPA). We will also hear from speakers representing the industrial, environmental, and academic sectors. This afternoon we will subdivide into discussion or syndicate groups whose topics reflect the major concerns raised in the written comments on the draft regulations. As participants here you will be asked to discuss these issues and where possible develop some consensus on approaches to be taken to resolve problems that have been identified. You were asked to sign up for these syndicates when you registered. If you haven't done so, would you please sign up during the coffee break?

There are some logistical things I should mention. Tomorrow morning we are expected to be here about 8:30 for a short plenary session before syndicates resume. If we have time following this morning's presentations, questions from the floor will be welcome. Those addressing questions to the speakers are asked to move to the microphones and identify yourselves. This will aid both the translators and those preparing the proceedings of the workshop.

Our first speaker this morning is Dr. John Buccini who will comment on the objectives of the regulations and provide us with some of the background leading up to this workshop. John is a native of Winnipeg and received his university education at the University of Manitoba, completing his Ph.D. in chemistry in 1970. Following postdoctoral work at Carleton University, he joined Health and Welfare Canada in 1972 and, over a 10 year period, was involved in: assessing the health hazards, setting up guidelines, and administering the former Environmental Contaminants Act. He moved to Environment Canada in 1982, and was subsequently involved in the preparation of the Canadian Environmental Protection Act (CEPA). Dr. Buccini is currently the Director of the Commercial Chemicals Branch which is tasked with administration of several of the toxic substances provisions of CEPA including the development of regulations for the notification of new products of biotechnology.

Our next speaker is Dr. Terry McIntyre, also of Environment Canada, where he is Head of the Biotechnology Section in the Commercial Chemicals Branch. Terry received Bachelor degrees from the University of Western Ontario and the University of Waterloo, his Master's from the University of Guelph, and just this year his Ph.D. from the University of Waterloo. Terry was the first co-chairman of the federal government Working Group on Safety and Regulations in Biotechnology. He is also a member of the OECD Expert Working Group on Safety and Regulations in Biotechnology.

Health and Welfare Canada's role in CEPA will be addressed by Dr. John Smith who is Head, Biotechnology Section in the Environmental Health Directorate. John is part of the group fulfilling H&WC's responsibilities under CEPA and has been involved in the development of biotechnology regulations since 1988. Prior to this, Dr. Smith was with the Ministry of Health and the Ministry of Natural Resources in Ontario.

Following Dr. Smith and presenting an academic perspective on the CEPA regulations will be Dr. Cam Wyndham. Dr. Wyndham is a graduate of McMaster University with advanced degrees from the Universities of Guelph and Calgary. Dr. Wyndham is presently an Associate

Professor at Carleton University, Ottawa, where he is actively engaged in research on bioremediation of toxic organics in the environment. In this respect, Dr. Wyndham has first hand insight on the concerns of the scientist in undertaking environmental biological research under the umbrella of CEPA.

Today, to discuss the United States Environmental Protection Agency's perspective on biotechnology, we are fortunate in having Dr. Larry Zeph. Dr. Zeph is with the Office of Toxic Substances, EPA, where his duties include coordination of scientific assessments of proposed commercial uses of genetically modified organisms and liaising with other federal agencies on biotechnology policy issues. Dr. Zeph is well qualified in this area having obtained his Masters and Ph.D. degrees from Pennsylvania State University in molecular and cell biology with emphasis on microbial activities in soil. These lines of investigation were continued for a number of years at New York University, where he investigated the physical and biological parameters affecting gene transfer in the soil environment.

Following Dr. Zeph, we have Mr. Paul Muldoon. Paul is the Project Director for the Canadian Institute for Environmental Law and Policy. He is also Program Director and Counsel for Pollution Probe. He has written a number of articles on various matters relating to biotechnology and other environmental issues. He has an M.A. from McMaster University and a Master of Laws from McGill. Paul will address us from the environmentalist's standpoint.

Industry will have the chance to have its say in our final talk of the morning. In Canada the biotechnology industry, still somewhat fledgling, is represented by the Industrial Biotechnology Association of Canada. This morning, we have the President of that association here to address us. Mr. Rob Quinn spent some time in the federal public service with External Affairs, Department of Regional Economic Expansion, Fisheries, Environment and Industry Trade and Commerce. He also spent some time as an executive with the Canadian Association of Broadcasters and has consulted privately since. He is probably better known locally as a sometime Alderman in the City of Ottawa and a sometime Councillor, Regional Municipality of Ottawa-Carleton. At the moment however, he is President of the Industrial Biotechnology Association of Canada and it is in this capacity he will address us today.

Syndicates and group discussions play a major role in working meetings of this type. Just before we break for lunch, Dr. Sheila Forsyth, who has played a major role in the organization of this workshop, will outline the the topics to be covered in the syndicate groups, where your particular meeting rooms will be, and the agenda we will be following for the next day and a half. Sheila studied at Carleton University where she received her Bachelor's and Master's degrees. She obtained her doctorate from Macdonald College of McGill University and followed this with a postdoctoral stint at Agriculture Canada's Regina Research Station. Prior to transferring to Environment Canada in the spring of 1990, Sheila was involved in the development of guidelines for microbial and other biological pest control agents with the regulatory arm of Agriculture Canada.

THE CANADIAN ENVIRONMENTAL PROTECTION ACT AN INTRODUCTION TO THE REGULATIONS

Dr. John A. Buccini, Director
Commercial Chemicals Branch
Environment Canada

Thank you, Keith and good morning, ladies and gentlemen.

I'm going to take a few minutes of your time this morning to orient you with the placement of this consultation meeting in the overall process of trying to develop regulations for notification of new biotech products. Before I do this I would like to thank you all for coming this morning, a particularly cold morning, though I sense the subject matter may cause things to warm up as the day goes on. I would like to first of all acknowledge our colleagues from the US Environmental Protection Agency who have taken the trouble to be with us even though it is one of their national holidays. We appreciate your effort and are looking forward to your contributions. Thanks, of course, are due to each and every one of you. It is with this type of participation that we hope to achieve an improved product as we move towards our regulations.

We are moving towards a regulatory scheme for biotech products and this will come under CEPA which is a joint responsibility of Health and Welfare Canada and Environment Canada. While in many cases you will be receiving correspondence under Environment Canada letterheads this simply indicates that EC is the administrator of the Act. In fact the decision making is a joint responsibility; Health and Welfare Canada for the health aspects, and Environment Canada for the environmental impacts.

Just a few words on multi-stakeholder consultations: Environment Canada and Health and Welfare Canada have had a number of years practice with this, going back to about 1985 when there was a formal commitment to this mode of consultation. It started out with amendments to the Environmental Contaminants Act and it has rolled over into the Canadian Environmental Protection Act consultations and discussions, and we have found that it is something which leads to an improved product. Just to encourage you to share fully your views, they are valued. We have our staff here to present and explain the proposals but most of all, we are here to listen to your comments. We have not cornered the knowledge market within government and we are looking for inputs, so please provide them.

I'd like to make a couple of comments on the regulations themselves. The objective of the regulations is to guide the development of the biotechnology industry in such a way as to allow the economic development of this new technology to take place, while addressing the need to protect public health and the environment from potential risks that could accompany this development. We cannot afford to repeat the mistakes that were made in underestimating the deleterious effects that accompanied the growth in the manufacture and use of chemicals following the Second World War. The public has expressed rather clearly their dissatisfaction with the way in which governments have failed to provide the public with an adequate degree of protection from this chemical threat. We are trying to turn this around in the next five years or so with CEPA and various government programs. We should learn from our past mistakes and with biotechnology referred to as part of the third wave of the Industrial Revolution, I think we have a responsibility to ensure that, while the industry is on a growth

curve, we are anticipating and preventing problems as opposed to waiting for them to happen and then trying to figure out what to do after the fact.

The last point I would like to make in regard to these regulations is that they are a priority of the federal government. This is evidenced by the explicit reference to the development of a regulatory program to guide the biotechnology industry in the government's Green Plan that was released on December 11, 1990.

This present meeting that you are attending today and tomorrow is the concluding phase of consultation that began in October, 1990 with the release of some three thousand copies of the most recent draft regulations for public review. From this we have received over four hundred responses. These comments have been analyzed and it is a reaction to these comments that has established the agenda for the next two days. So the purpose of this meeting is to review the dominant concerns that surfaced from the comments received. Following the completion of your discussions, a Proceedings of the Workshop will be produced which you'll all receive in time.

At the same time, with the conclusion of this phase of the consultative process, the output of your discussions will be taken into account in the redrafting of the regulations. It is my expectation that the new draft of the regulations will be the subject of one more phase of consultation prior to proceeding to the Canada Gazette Part I for the formal legal consultation on the proposed regulations. This will depend on how well we do our job in the next couple of days.

I would remind you that the Green Plan does call for this set of regulations to be in place by 1992. It is therefore a task for us in the federal government to achieve this through soliciting public input and taking into account the many scientific and technical aspects of the issue as well as intergovernmental concerns, both federal-provincial and international.

I reiterate that your views are valued. I encourage you to participate fully in the plenary and working group discussions. It is important that we identify accurately the essential issues that require resolution and, to the extent that you can do so, recommend solutions to these issues.

Our ultimate objective is to have in place a set of regulations that provides a means to assess the potential risks that may accompany the manufacture, importation, use, or release of new products of biotechnology. This set of regulations must be technically sound, and be seen by the public as responsible and responsive to the issues.

I wish you well in your discussions and I assure you that what you generate in this meeting will be factored into the next draft of the regulations.

THE DEVELOPMENT OF CEPA BIOTECHNOLOGY REGULATIONS

Dr. Terry C. McIntyre
Head, Biotechnology Section
Commercial Chemicals Branch
Environment Canada

Thank you very much, Keith. I would like to add my own words of welcome this morning to those given by Keith Bailey and John Buccini. We look forward, over the next two days, to your insight in terms of how information gleaned from syndicate discussions can be best utilized by us towards the further development of the CEPA biotechnology regulations. As Dr. Buccini has indicated and as many of you are aware, the design of a regulatory oversight mechanism is not an easy task. We are, however, guided in this workshop by our previous experiences in the regulatory arena that have demonstrated unequivocally that a consensus building process involving all affected stakeholders can be a powerful and effective tool for the establishment of an appropriate regulatory framework.

In discussing the environmental components of the CEPA biotechnology regulations this morning I'd like to examine with you three key components that have influenced both the structure and methodological approach proposed in our draft regulations.

Our proposed biotechnology regulations are based on the elements featured in Table I which underlie the legislative framework for CEPA.

TABLE I

CEPA AND THE LEGISLATIVE FRAMEWORK FOR ENVIRONMENTAL PROTECTION

- STRONG PREVENTION FOCUS
- LIFE CYCLE APPROACH TO MANAGEMENT OF TOXIC SUBSTANCES CRADLE TO GRAVE
- SHIFT OF ONUS OF PROOF TO MANUFACTURER/IMPORTER
- INTEGRATION OF ENVIRONMENTAL AND HEALTH REPORTING
- AN ECOSYSTEM APPROACH TO ENVIRONMENTAL PROTECTION
- NATIONAL INSPECTION PLAN AND ENFORCEMENT POLICY BASED IN CRIMINAL LAW
- EXTENSIVE PUBLIC ROLE IN THE ADMINISTRATION OF THE ACT
- INNOVATIVE MECHANISMS FOR FEDERAL-PROVINCIAL PARTNERSHIPS
- ENFORCEABLE STANDARDS FOR FEDERAL LANDS, WORKS, AND INITIATIVES
- ENVIRONMENT ECONOMY LINKAGES AND ENVIRONMENTAL QUALITY OBJECTIVES

The draft regulations acknowledge criteria generally recognized as essential components of a regulatory framework for biotechnology. They include such considerations as a regulatory

structure that includes the components of Table II.

TABLE II

CRITERIA CONSIDERED AS ESSENTIAL COMPONENTS OF A REGULATORY FRAMEWORK FOR BIOTECHNOLOGY

- ENGENDERS PUBLIC CONFIDENCE
- MAKES ECONOMIC SENSE
- FACILITATES INDUSTRIAL PLANNING FOR DEVELOPMENT
- COMPATIBLE WITH INTERNATIONAL APPROACHES
- FLEXIBLE AND ACCOMMODATING OF NEW APPROACHES
- CLARIFIES JURISDICTIONAL RESPONSIBILITIES
- DRAWS UPON INDEPENDENT SCIENTIFIC ADVICE

Our regulations in Canada also acknowledge certain working principles that have evolved in the international community for the regulation of biotechnology products that include those outlined in Table III.

TABLE III

FEDERAL GOVERNMENT WORKING PRINCIPLES FOR THE REGULATION OF BIOTECHNOLOGY PRODUCTS IN CANADA

- USE OF A STANDARD DEFINITION OF BIOTECHNOLOGY
- BUILD UPON EXISTING LEGISLATION WHEREVER POSSIBLE
- REGULATE PRODUCT AS OPPOSED TO PROCESS
- ASSESS BIOTECHNOLOGY PRODUCTS ON A CASE-BY-CASE BASIS
- BUILD UPON INTERNATIONALLY DEVELOPED GUIDELINES AND HARMONIZATION WHENEVER POSSIBLE AT BOTH FEDERAL AND INTERNATIONAL LEVELS

General Provisions

I would just like to spend a few minutes on the general provisions of the regulations.

- Products assessed under the proposed regulations include microorganisms to be used in a variety of applications such as, but not limited to, bioremediation, mineral leaching, degradation of chemicals, mining, waste treatment, waste disposal, chemical production, lignin

degradation, microbial enhanced oil recovery, biosensors, and energy production.

- An iterative and staged approach to notification and provision of information is used, based on the stages of development of the product towards commercial exploitation. The corresponding information requirements and assessment periods build on those of previous stages of notification.
- Notification is required prior to manufacture or importation for contained uses beyond the scale of laboratory research.
- Information will be assessed within prescribed assessment periods.
- CEPA contains explicit provisions for protecting confidential business information.
- The waiver provisions of CEPA provide flexibility for dealing on a case-by-case basis with specific products where the progression through the stages is either not appropriate or necessary, or for waiving information requirements that may not be applicable for the product.
- A mechanism is proposed for listing specific uses of microorganisms for which notification would not be required (Schedule XVI).

Categories for Notification

Five stages of development are defined for notification.

For contained use, notification is required:

- prior to research and development beyond laboratory scale (Schedule XI).
- prior to commercial manufacture (Schedule XII).

For environmental introduction, notification is required:

- prior to small-scale field trials (Schedule XIII).
- prior to large-scale field trials (Schedule XIV).
- prior to commercial production (Schedule XV).

Information Requirements

Each of the five information schedules specify the applicable information requirements. Categories of information to be submitted include:

- identification and characterization of the microorganism(s)
- data on environmental fate and effects on nontarget substances in the environment

- human health safety testing data
- description of intended uses, manufacturing methods and quality control and quality assurance procedures
- specifics on field trials including location and procedures to be used during the trial, where applicable.

Closing Points

In the development of the CEPA biotechnology regulations, we recognize that a properly drafted and administered regulatory framework can be a catalyst not an impediment to technology development.

We recognize the need for flexibility in addressing the needs of the dynamic and expanding biotechnology industry in Canada. The flexibility we are building into the regulations is linked to and dependent upon information on both human health and environment. Environment Canada is funding and will continue to fund, basic research in microbial ecology addressing such questions as:

- mechanisms for gene exchange in the environment
- development of methods for detection, monitoring, and determination of environmental fate of microorganisms
- identification of factors/characteristics that affect survival, persistence, and dissemination of microorganisms in the environment.

The data generated by our research program will not only assist us in our regulatory program but will be a source of valuable scientific information on the behaviour of microorganisms in the environment for industry, academia, and other government departments alike.

We constantly seek to promote national and international cooperation and information exchange in biotechnology through our involvement in a number of interdepartmental committees under the National Biotechnology Strategy, the Organisation of Economic Cooperation and Development (OECD), the United Nations Environment Programme (UNEP), federal-provincial regulatory consultations, and more recently, under a memorandum of understanding we have with the Environmental Protection Agency in the United States.

We believe that we are establishing a sound and responsive health and environmental oversight structure for biotechnology in Canada under the Canadian Environmental Protection Act and actively encourage your comments over the remaining two days as to how you feel the process can be improved and changed.

THE ROLE OF HEALTH AND WELFARE CANADA IN CEPA

Dr. John Smith
Head, Biotechnology Section
Environmental Health Directorate
Health and Welfare Canada

I. Introduction

I would like to add to the welcome which has already been extended. As noted previously, we are hoping that this workshop can provide some suggestions on how to approach the major issues that are coming to light in the early part of this consultation. Based on the outcome of this workshop, along with comments already received, we will have an opportunity to identify both areas of agreement and areas of contention, and plan appropriate ways to address those concerns. We look forward to the discussions over the next two days and the continued dialogue that will follow.

Under CEPA, as Dr. Buccini has mentioned, the Department of National Health and Welfare is jointly responsible with Environment Canada for developing notification requirements for new biotechnology products. The draft notification scheme that is the subject of this workshop is intended to allow for a meaningful first assessment of these substances. Under the notification process, the Environmental Health Directorate will be assessing the information provided to determine if there are adverse health impacts and what controls, if any, may be needed. Staff from the Environmental Health Directorate, National Health and Welfare, are present at this workshop to hear the recommendations that you are going to provide in order to guide our efforts over the coming months.

In addition, officials from other areas of the Health Protection Branch are present. Many are or will be dealing with regulatory issues concerning biotechnology in programs that CEPA will complement, and are present to hear the discussions that will ensue among the experts that have assembled here. We will be working closely with these officials, through departmental and interdepartmental groups devoted to biotechnology, to ensure a cohesive, consistent approach, that will lead to safe development and use of the products of this important technology.

II. Development of health data requirements

To provide some background to the development of information requirements in the current draft, it is necessary to look at the development of the legislative framework we are using. The relevant parts of CEPA were developed after a detailed consultation that reached agreement on how to implement notification and assessment of a minimum data package for new chemicals, based on OECD guidelines. At the time of that consultation, it was recognised that products of biotechnology should be included in the process, but the questions of how to structure the notifications for biotechnology products, and what would constitute an appropriate data package, were not addressed. Essentially, then, the draft notification requirements for biotechnology products have been developed within existing legislation (albeit not long-standing) that was developed for chemicals.

In considering the draft requirements, then, you will need to examine both the notification framework that is being proposed, and the information requirements that will be necessary for a meaningful health and environmental assessment of the products.

The main features of the notification requirements [as outlined previously] are two steps:

> Manufacturer or importer of a new substance is required to provide information on the substance and wait for the assessment period to expire. Both the information required and the length of the assessment period are prescribed in regulations.
>
> Health and Welfare Canada and Environment Canada are required to assess the information within the prescribed assessment period.

Any action, including requiring further information or imposing controls on the substance, is contingent on demonstrating that there is a suspicion that the substance is "toxic" based on that first assessment (in the way "toxic" is defined under CEPA).

You will note that this process is not a licensing or registration process, as occurs with some other products subject to regulatory review. Limits on the use of a substance may come only after assessment and suspicion of toxicity.

Therefore, in determining the information that would be necessary to evaluate a new biotechnology product, we needed to specify a schedule of data that could be used to make a reasonable judgement on a wide variety of organisms, products, and uses. There is not a mechanism to require more data simply because we do not have enough data to make a judgement in a particular case.

We can, however, waive information requirements in particular cases, for example when the information is not needed to assess the substance, when it is not technically feasible to provide the information, or when it can be demonstrated that the substance will be adequately contained to protect human health and the environment.

III. Use of pesticide information requirements

Under these circumstances, it was decided to base the human health and safety information requirements on those developed for microbial pesticides. These requirements provided a system that was both available and that should provide sufficient information for a meaningful assessment.

It is recognised that all the data requested may not be applicable in every case. Under the present draft, there is a mechanism, through waivers of data requirements, to tailor the information requirements to specific uses.

At some point, it may be possible to define specific categories of microorganisms, for example based on their use, and to develop data requirements specific to those categories. The current draft only deals with use categories in a very broad way, i.e. contained use vs. environmental introduction.

I would point out that the intent of the draft regulations was to define "contained" in only a general way that would indicate that an organism was being limited from general environmental release. Specific containment measures, if required, would be determined after assessment of the information. However, it is also expected that waivers of some data will be requested, when evidence of appropriate "containment" can be provided, again using the

word in a general sense. This follows one of the waiver mechanisms specifically provided for in CEPA. The syndicate on contained manufacture will, I'm sure, be able to provide useful suggestions in this area including how to appropriately reference existing "containment" guidelines.

IV. Comments requested

What would we like to hear from you? The simple questions (at least in the asking) would be: What information is necessary to provide a meaningful assessment of potential human health and environmental impacts of a microorganism developed as a biotechnology product? And what improvements can be suggested to the notification framework that has been developed under CEPA?

It is clear, both from our work and from the written comments received, that the answer to the question of information required cannot be separated from the question of which organisms, and which uses, should be assessed.

Nevertheless, to the extent possible, it would be particularly useful to us if the discussions, at least in the Health Data syndicate, could assume that you are talking about organisms that will require notification and assessment, and then discuss what information should be assessed. Some suggested topics to address include what endpoints should be considered in relation to human health? What alternative testing strategies are available? An important area is how existing information about a microorganism should be integrated with specific test requirements.

The issues of scope of the notification requirements and means of dealing with contained manufacture are important and will be addressed in specific syndicates.

In addition, the draft notification requirements were developed with single, identifiable substances (i.e. microorganisms) in mind. The syndicate dealing with microbial consortia will be discussing the interesting and difficult question of how to extend this approach to mixtures of microorganisms.

V. Closing

In closing, let me repeat that we in Health and Welfare Canada and Environment Canada are appreciative of your comments and the time you are taking to come to this workshop. We look forward to hearing your discussions, and receiving your recommendations. We also look forward to the further consultations that will help refine our requirements. In the end, they will be an important mechanism for ensuring that the benefits of this exciting technology can be achieved in a way that ensures safety to health and the environment.

Keith Bailey, Chairman: -- We are running about five minutes ahead of schedule which is a little bit unusual for meetings of this sort so we do have the opportunity for a limited number of questions. I would remind you that we do have simultaneous translation and again, if someone has a question, please use the microphones and identify yourselves.

Any questions that you wish to address to Dr. Smith or Dr. McIntyre at this time?

Cummins: -- Yes, I would like to comment on field tests and releases which have already taken place. As you know there have been extensive releases, field tests of transgenic

organisms, principally plant materials presumably, as well as microbes. These have been undertaken without regulation, as far as I can see. One of the most interesting examples I have recently seen is the situation with an indicator gene called GUS which is a bacterial product introduced into corn crops. When this was field tested at the University of Western Ontario it was released to the environment and, I think, indiscriminately. The Minister of Agriculture came back to me and said, "Yes we acknowledge that this indicator gene from a microbe, transgenic to the corn, has been released and may, in fact, inhabit commercial corn crops because of the field testing procedures." He says now to me, I must prove that GUS is unsafe for humans. I had understood that transgenic products needed to be tested to determine whether or not they were unsafe. The burden of proof he shifted back onto my shoulders. What I say is that kind of, to me, sleazy approach to regulations, needs to be considered seriously. Sleazy because it shifts the burden of proof to proving things to be unsafe to the population in general, who have no resources in this regard, away from the government which I think should be saying "these things are safe." Now you say you must need suspicion of hazard and I say to you I need, or I demand, assurances of safety. The burden of proof you see...and again suspicion of hazard....not suspicion, but assurances of safety is what is required.

Smith: -- In terms of CEPA, we are primarily here to discuss our own regulations. The suspicion of toxicity is the trigger that lets us go into a number of further actions, including control, assessment for further information, and so on. One of the things I was trying to point out, that in developing our regulations we are looking to requiring sufficient information about any products that fall under our jurisdiction to give us enough information to allow us to make a judgement as to whether or not there is a suspicion of toxicity. It's an improvement over the previous legislation for chemicals where the burden of proof was on the government to determine the suspicion before we could require any information. The approach under CEPA is that we require the manufacturer or importer of products falling under our jurisdiction to provide the information up front. A lot of the discussions that will ensue today will hopefully come to some agreement on what is a reasonable amount of information.

In terms of the specifics of the case that you mentioned, I am not sure that we are here to discuss specific products and regulatory decisions, but we will find out that it is not a one department or a one legislation business in the regulation of biotechnology. There are a number of people involved and we're all working through an interdepartmental coordinating mechanism to make sure that we cover all bases. In this sense CEPA is a very important mechanism in that it has the capacity to fill in any gaps that might exist in the rest of the framework.

Comeau: -- I would like to caution the regulatory organizations against the public feeling that for example, microbes are evil, and viruses are evil *per se*. There are special cautions to that. You know you are eating yoghurt, cheese, drinking beer, and animals sometimes do things that are intrinsically very strange. For example, rabbits eat their own faeces and if you prevent them from doing that they are going to die. There are a lot of microbial contaminants in food that is already being eaten. The nuclear polyhydroses viruses that are used to fight insects, for example, on which the regulation problem has cost an awful lot of research money; people have been eating these viruses all along without any problems.

I think at some point there's going to be a need for more public discussion with scientists because in certain things I think we are losing some common sense. On the other hand, I do realize that the risks are not necessarily what the public believes. There are certain risks and because of these, steps have to be taken so things that are really dangerous are regulated. Transgenic organisms are not necessarily dangerous at all. In fact, they could be the solution to a lot of environmental problems that exist right now. If the burden put on the people developing these transgenic organisms is too high, and you must remember that the budget

for research in this country is quite small, if the burden is too high, we are going to prevent the scientist from developing solutions to the problems that have been caused by the chemical approach in many cases, such as in pest control. If we are going to do this, the environmental problems that we have because of chemicals, are going to keep increasing. Problems are going to get to the point where they cannot be cured.

McIntyre: -- You've raised a number of issues André (Comeau) and I think that it is important to recognize that the development of the regulatory oversight for biotechnology is precipitated not only from the potential for problems to arise that are inimical to human health and the environment but also from previous experiences associated with the introduction to society of new technology particularly in the nuclear and chemical areas. We're very sensitive to some of the concerns you have raised and I am looking forward to seeing how some of those concerns might be addressed over the next two days.

ACADEMIC PERSPECTIVE ON THE PROPOSED CEPA REGULATIONS

Dr. R. Campbell Wyndham
Department of Biology
Carleton University, Ottawa

I want to thank the organizers for inviting me to this session. I am going to present a perspective which I hope will be representative of other academics like myself in similar positions in Canada, microbial ecologists or perhaps other academics who might not call themselves microbial ecologists but nevertheless are influenced by the field and are interested in the activities of microorganisms in natural environments. There are perhaps two or three dozen labs in universities across Canada with research programs and students who are involved in environmental release experiments or who are at least poised to carry out environmental releases of microorganisms. These laboratories are interested in establishing the groundwork, establishing the important information on microbial ecology, that we require for these regulations to work.

There are, from an academic perspective, two research practices which will be most affected by the regulations and which will influence the laboratories that I have mentioned. These are the areas of:

13(1)(a)	1. Large-scale fermentations within contained laboratory facilities
13(1)(c)	2. Small-scale field trials for the purposes of establishing ecological properties of a biotechnological product.

I am not going to say very much about the first area because I haven't had too much experience with large-scale laboratory fermentations. I will have more to say about the small-scale field trials.

As a microbial ecologist, I and my graduate students, work in the area of bioremediation of toxic organics and gene transfer in the environment. This type of study is fairly representative of 40 to 50 researchers in Canada who, as I have said, may not call themselves microbial ecologists but are nevertheless influenced by the field.

We work in a laboratory in which we grow cultures of organisms isolated from the environment. We isolate proteins, membranes, or plasmids; we prepare antibodies or DNA probes. We release up to 10^9 microbes per day...in fact the laboratory is a Level 1 containment facility in keeping with the MRC guidelines. Obviously the objective of much of our work is to understand how microorganisms function in environments outside of a Level 1 laboratory. In our case, with the bioremediation of toxic organics, we have initiated "academic scale" field trials. We are, in fact, in common with a number of other laboratories in Canada, at the juncture of moving from a Level 1 containment laboratory to the environmental release of some of our products (Fig. 1).

I think the new regulations will have an important effect on this type of research, i.e. small-scale field trials and large-scale laboratory fermentations. I hope to point out in this overview

how the regulations will have a positive influence and will promote research in microbial ecology. We definitely need solid information on the effects of microorganisms in complex microbial environments: the effects of organisms on community structure, biogeochemical cycling, microbial interactions, gene transfers, and a number of effects and processes which we really do not understand clearly at the moment.

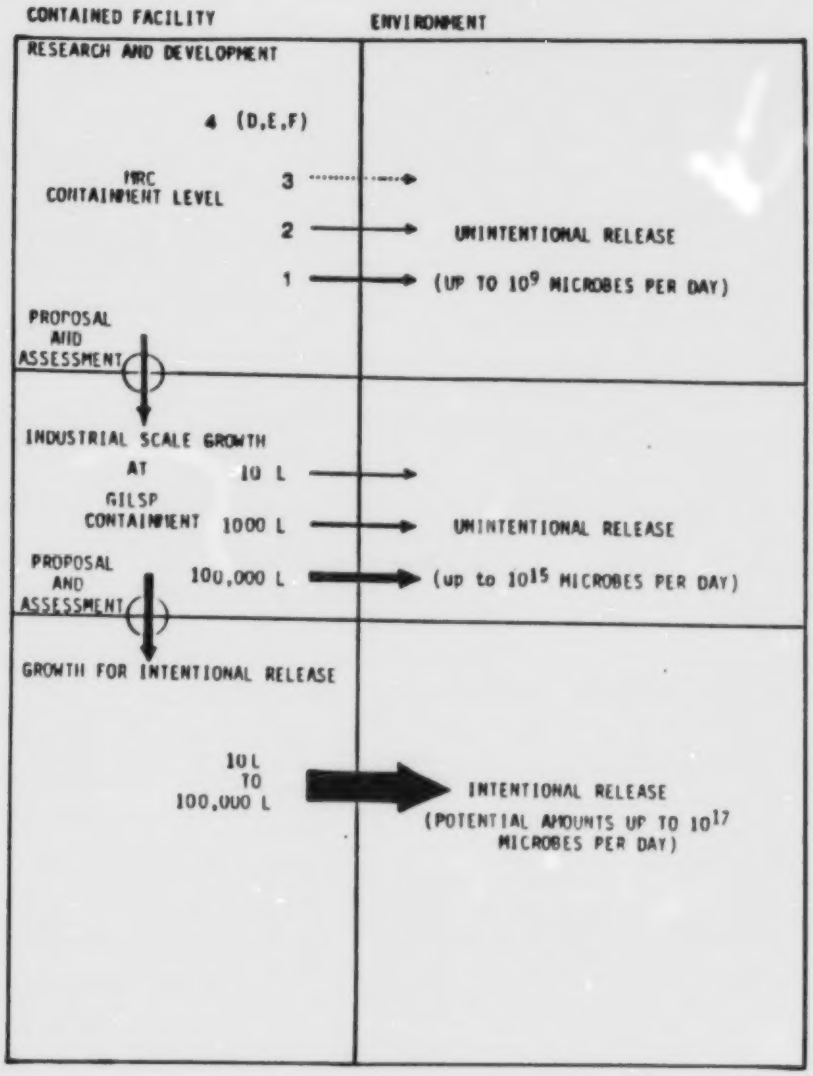
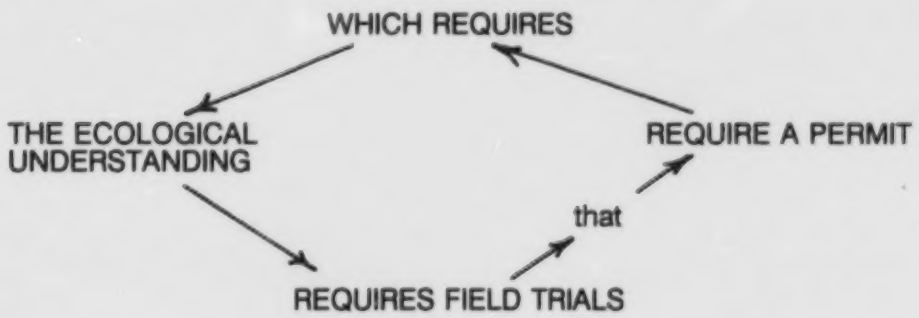


Fig. 1. Environmental Release

The second thing I hope will come out of these regulations is that they will be flexible enough to allow field trials to proceed (small-scale) without an enormous amount of pre-trial information required. By this I mean the ecological factors, according to the regulations now, must be at least partially understood and must be put into these proposals for a small-scale release. Yet, that same information can only be provided by doing the type of trial in question. What I am pointing out is that we must be very careful not to paint ourselves into a corner or become so restrictive that we are not allowed to carry out the types of ecological

studies that we need to do in order to provide the information for proposals for larger scale releases.



In terms of the two areas I pointed out in the beginning, the laboratory large-scale fermentations, and the small-scale field trials, which are most important for our economic studies? The first of these, the large-scale laboratory fermentations in the proposed regulations, and if you'll look at the length of Schedule XI in comparison with Schedules XIII, XIV, or XV there is a fairly limited amount of information required that should not be too onerous to provide before large-scale laboratory fermentation. I would particularly point out that there is limited toxicity testing required in order to carry out large-scale fermentations within the contained facility. I think the most important part of Schedule XI which covers that type of activity is that it will ensure that an active and effective Biosafety Committee is in place. As I've said, large-scale fermentation is not my particular interest, so I will not say any more on this area.

If you will bear with me, I am going to use an example, a case study of a small-scale field trial, in order to point out what I think are the important factors in the proposed regulations.

We are interested in microorganisms that degrade environmental contaminants and using them in open applications, in small-scale field trials, and in waste water treatment facilities which are obviously open to the environment. Our recent studies have been with an organism that degrades chlorinated aromatic compounds. And I'm going to show you some of the background for this example and illustrate where in the Schedules we may have run into difficulties. This is an organism we have called *Alcaligenes* sp. BR60 and right away we are in difficulties with the proposed regulations; what is in a bacterial name?

We've been unable to identify this organism to species level because it doesn't fit with any particular species of alcaligenes. So we know its genus but not its species. We also know from DNA homology studies that the general area that the bacterium falls into is a ß-proteobacterium or a Group III Pseudomonad group. This is as far as we've been able to type it. We could go through the difficulties of assigning a species name to the organism but we don't feel that it is worth the effort. As it stands, our proposal would probably suffer because of the poor identification at the moment. Nevertheless, it has very interesting properties which we would like to use in bioremediation and this is one of the issues that we have to address, the identification issue. We have an organism that is well identified in a sense but because it doesn't have a name we are disadvantaged.

The organism was isolated from the Niagara River near a toxic chemical landfill in New York State. It was selected on the basis of its ability to degrade chlorinated aromatics. The reason it is an effective degrader of these pollutants is that it carries a highly mobile genetic element which specifies the degradation of these chemicals.

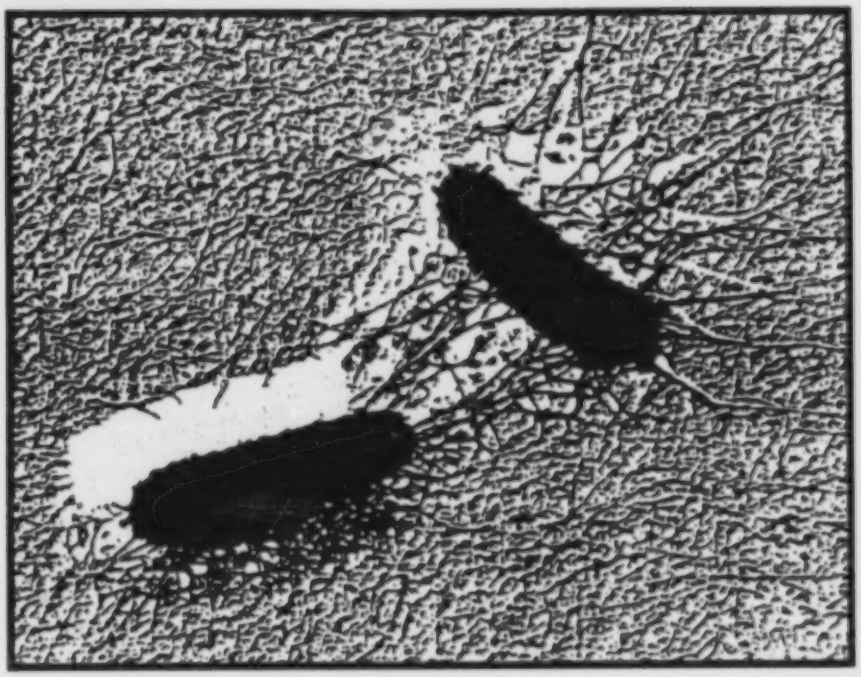


Fig. 2. *Alcaligenes* sp. BR60

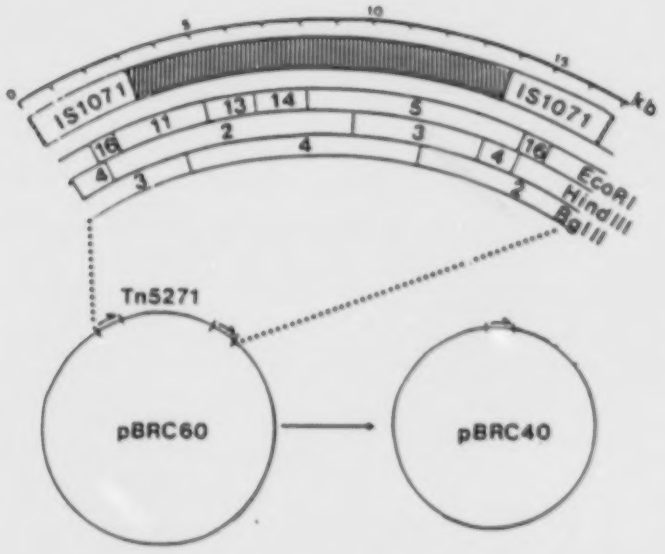


Fig. 3. Genetic (restriction digest) map of the 3-chlorobenzoate catabolic transposon Tn5271 from *Alcaligenes* sp. BR60.

I've pointed this out for another reason. This organism depends on the ability to reshuffle and mobilize its genes in order to be effective for the degradation of environmental pollutants. This raises another set of difficulties. The regulations are implicit in a requirement for genetic stability. In this particular instance this would create problems in terms of using this organism in the environment. This organism is not, as I would like to point out, genetically engineered. It effectively genetically engineers itself, using insertion sequences and transposable elements.

This research has been carried out by a graduate student under the proposal "to investigate the influence of contaminant exposure on the survival, activity, and transfer of a catabolic genotype," and in a moment I will go into the schedule she used for the study. First of all, the study in general...she took this organism from the Niagara Region, transplanted it to the Rideau Canal system, and carried out the studies at the Queen's University Biological Station on Lake Opinicon. So we are taking a natural organism from one site, rearing it and determining genetic structure and phenotype in the laboratory, and then transplanting it to a new environment. The new environment was the Lake Opinicon Biological Station on the Rideau system. The work was carried out in the toxicology facility, a ten by ten shack, and by no means contained at any level.

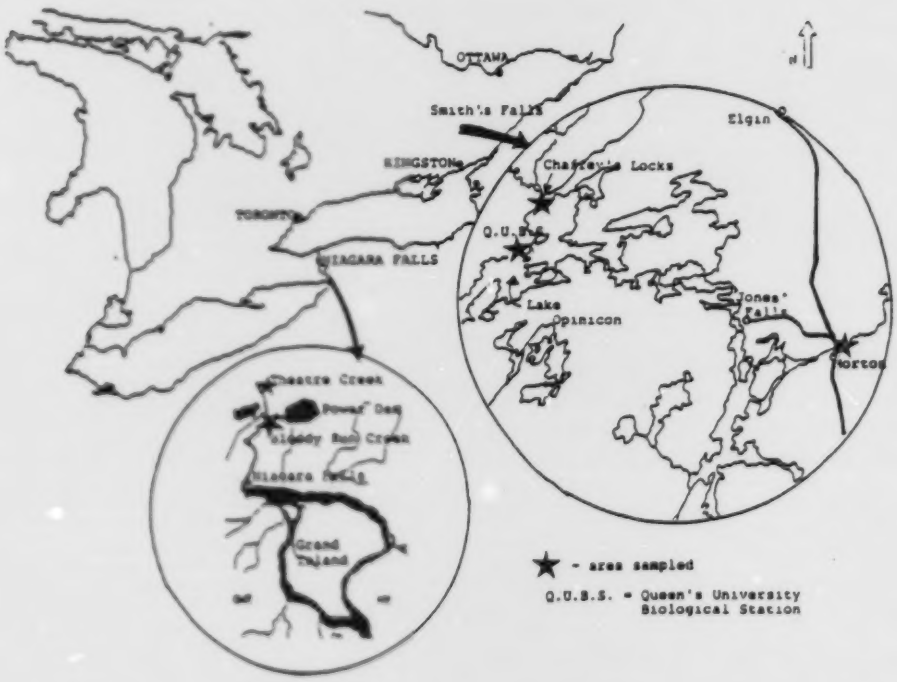


Fig. 4. Sites sampled for *in situ* colony hybridization with pBRC probe

The organism was studied in flowthrough microcosms in this laboratory. Because of the nature of the system it was not contained and there were some 600 L/day going through and this amount could not be sterilized. The output from this trial was carbon filtered to a seepage bed and then directly to the lake (Fig. 5).

Now clearly this type of a study represents a small-scale field trial because it is done outside of the confines of the laboratory.

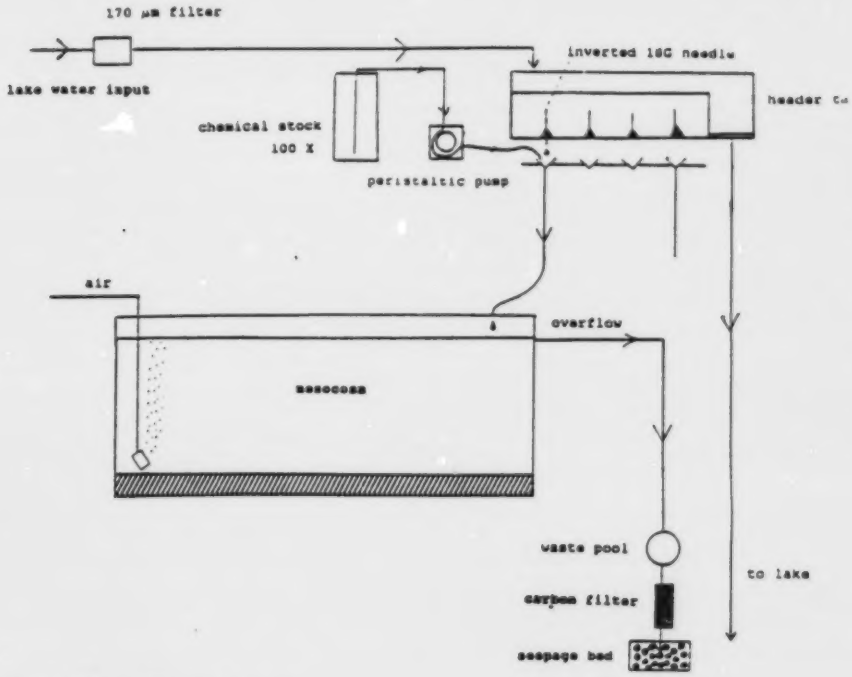


Fig. 5. Experimental setup.

If we go through the regulations and look at the Information Requirements for this type of a study we find the following (Fig. 6):

13.(1) Any person who manufactures or imports a microorganism that is not specified on the Domestic Substances List shall provide the Minister with the following information:

(c) where the microorganism is manufactured or imported for **environmental introduction in a small-scale field trial,** the information specified in Schedule XIII;

15. The prescribed date before which;

(c) the information referred to in paragraph 13.(1)(c) shall be provided, **is 90 days** before the day of manufacture or importation of the microorganism commences;

Fig. 6. Information requirements

This information would have to be provided 90 days beforehand. In retrospect I wonder how we would have supplied the information.

First of all, identification; I have already pointed out the difficulty there and I don't think that ours will be an isolated case. I think that we will find with many organisms which will be used for small-scale field trials for mineral leaching, bioremediation and what have you, that we will run into cases where some very useful organisms cannot be identified because of inherent descriptive difficulties or because they fall outside the known species designations. This is something I think we should address in the next few days.

Other than these identification aspects, the information requirements of items 1 to 5 of Schedule XIII are not too difficult for us to provide for this organism (Fig. 7):

1. Identification
2. Phenotypic, genotypic and ecological characteristics
3. Genetic modifications and their detection
4. Intended use and manufacturing methods
5. Field trial design, containment and monitoring
6. **Ecological interactions and genetic stability**
7. **Microcosm test data, including toxicity, exposure, competitiveness, survival, dispersal, community interactions**
8. **Acute mammalian infectivity, toxicity and exposure**
9. Additional information
10. Other modifications

Fig. 7. Requirements for Schedule XIII

We know something about its phenotypic and genotypic characteristics. There are no genetic modifications for this organism so this presents no difficulty. The intended use is quite clear, and the field trial design, containment, and monitoring I think we had in hand, although perhaps not containment because we made no effort to contain the organism. We were able to monitor it effectively and our field trial design simulated a natural freshwater environment.

We do run into difficulties with 6, 7, and 8 of Schedule XIII. Ecological interactions and genetic stability were the objectives of the study (item 6). Specifically, we were to establish how the mobile genetic element transfers amongst bacterial genera. Obviously it is difficult to provide the requisite information before the fact.

The same holds for item 7 of the Schedule, which calls for microcosm test data, including toxicity, exposure, competitiveness, survival, dispersal, and community interactions. These requirements comprise the general objectives of our study. We did not have this information beforehand although we do have some of it now.

We initiated a study in January of 1987 and the first summer field trial was in June of the same year, so we had four to five months of preparation for the student to carry out the study. We had been working with this organism in the laboratory for four years before this, so we had quite a lot of information on it. Like most laboratories which are working on microbial ecology in the field, we had not tested our organism for pathogenicity, toxicity, or infectivity. Many organisms used in academic laboratories are isolated directly from the environment and I might also add that many organisms used in undergraduate laboratories fall into the same class and are worked on in a contained type of facility, for either research or teaching purposes, without mammalian testing or toxicity testing. We could provide that information, although we did not at the time.

Fig. 8 Time frame for field trials of *Alcaligenes* sp. BR60 to assess the survival, activity, and transfer of a bacterial catabolic transposon in a freshwater environment

R. Fulthorpe and C. Wyndham

Ph.D. student registration	January	1987
"Manufacture" of the organism	May	1987
Environmental release (10^{11} cells in 600 litres)	June	1987
Duration of the trial	June - Sept	1987
Subsequent field trials	June - Sept	1988
	June - Sept	1989
Ph.D. defence	January	1991

Acute mammalian infectivity, toxicity, and exposure, item 8 of the Schedule, presents difficulties in two ways. First of all, the timing. In our case, January to May was the preparation time. The first environmental release was in June and this was 10^{11} cells and about 600 litres. The timing was a factor. While we had 90 days, this was not sufficient to carry out the toxicity testing unless we wanted to lose that first field season. The other factor is cost. Funding for microbial ecology research is modest at best. For academic research budgets to have the additional burden of mammalian toxicity testing would be crippling. I hope when the situation merits it, that waiver provisions of CEPA can be used judiciously to prevent needless animal toxicity testing and limit it in low risk situations.

There are some factors that could alleviate the situation. Exemptions for low risk organisms is a subject which I hope we can spend some time on over the next couple of days. Can we define what organisms are going to necessitate mammalian toxicity testing? Are there groups we can exempt and on what basis can organisms be exempted? We are also in need of more relevant toxicity tests and this should be another area for discussion. One last point we might discuss is the question of repeat trials. We carried out the trial for three summers in a row and I wonder what the regulations will require in the case of repeat trials using the same organism or a slight variation thereof.

In summary, I suspect there are a dozen or more university researchers poised for field trials

of this nature...trials in areas as diverse as low-grade ore leaching to engineered biological control agents. Ideally we want to promote these studies. In the long run, they will provide the techniques and understanding in microbial ecology that we need to meaningfully fill out the requirements of section 6 and 7 of Schedule XIII; information on genetic stability, involvement in biogeochemical cycling, persistence, etc. I would also hope, when the situation merits it, that waiver provisions of CEPA can be used judiciously to prevent needless animal toxicity testing; and that the regulations themselves will promote meaningful experimental work in microbial ecology.

Melcer: -- Based upon the example that you have given, you could extend the example to any waste water treatment plant in the country where naturally occurring indigenous organisms are cultured essentially in a waste water plant to attack and destroy specific contaminants resulting from that particular industrial process plant. By implication would you think these regulations should apply to every waste water treatment plant in the country?

Wyndham: -- In my opinion that would be impossible and it wouldn't be necessary. There are mechanisms by which that type of application can be regulated.

Melcer: -- But it is really no different from the example that you have presented. You used an organism that was induced by the presence of land leachates from the Niagara River and you cultured it with the long-term objective of utilizing it to degrade chlorinated aromatics.

Wyndham: -- That is correct and it is those types of applications that we have to look at to decide just how much information we require on that type of organism.

Melcer: -- By inference these plants have been in existence for the past 50 years or so in many cases, and they have not caused any grief or death of individuals in the population. So why should we introduce regulations to control them right now?

Wyndham: -- I think maybe the distinction there is not necessarily the operation of a waste water treatment facility where a large consortium of organisms has been enhanced or enriched. I think we are looking ahead to the engineering or modifying of a particular organism and introducing it into the environment. I think these are two different things and maybe they should be considered differently in terms of the regulations.

Cummins: -- I disagree with the view that no harm has come from the manner in which sewage treatment proceeds. Certainly we have the appearance of many new totally antibiotic resistant forms of *Escherichia coli* and other major pathogens such that it leaves me to believe that impairment does occur and we should seriously consider these facts. So I think that any kind of fooling around with transposable elements and with the forms that are potentially pathogenic does require human pathological or some sort of mammalian toxicity testing in the long run. Now I think a lot of what is being done ignores the state of the art as well as technology. We can do insertions and sequence polymorphisms in fingerprinting particular forms of microbes and tracing their behaviour, very inexpensivley using PCR. These kinds of statements cannot be ignored any longer because we are fooling around with things that are capable of producing a lot of problems.

Wyndham: -- I think you are right in that sense. To take two extremes, if we isolate from a waste water treatment plant an enterotoxigenic *E. coli* we would certainly have to look at toxicity testing. On the other hand, long and expensive mammalian testing on an innocuous soil isolate could be totally unwarranted. I think we can come up with reasonable exceptions that do not need to be tested.

Polonenko: -- I'd like to comment on mammalian toxicity testing and the considerable costs associated with these tests. There are seven tests that are required: there are four acutes, two rotation studies, a hypersensitivity study. The requirements in Canada are somewhat more stringent than the United States and the additional work that is required triples the cost of these tests. What we are looking at for each organism is between three and five hundred thousand dollars to do these seven tests. If a laboratory that is going to be doing these toxicity tests is able to do them all at one time, then you need a minimum of ten men. If you are looking at these tests sequentially then you will need two to three years and possibly longer. That's what the implications of these tests are.

Hyzy:-- Just a couple of points as far as mammalian infectivity goes. You are asking for the introduction of these organisms by means which are totally artificial...intravenous or intra peritoneal injections of organisms that would certainly never occur in the field. And also, with the anti-vivisection movement coming on strong, I think we have to be very careful what experiments are necessary and what are not.

Bailey: -- Thank you very much and I am sure that regulatory departments are very sensitive to this particular question. At this point we will break for coffee and reconvene at 10:30.

THE EPA PERSPECTIVE ON BIOTECHNOLOGY

Dr. Larry R. Zeph
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Washington, D.C. 20460

For centuries, people have used living organisms to produce useful substances such as bread, cheese, beer, and wine, and more recently to perform useful functions such as the control of harmful insects. Initially, use of the organisms was empirical; however, over the centuries people have developed techniques to manipulate the genetic materials of useful organisms to select and enhance desired characteristics. Recently, powerful new techniques in molecular biology have been developed that permit the manipulation of the genetic materials of organisms in ways that heretofore were not possible, such as moving genetic material between organisms that would not normally exchange such material. Public awareness and concern that use of these new technologies may be associated with dramatic consequences have resulted in a call for some type of oversight to ensure adequate protection of human health and the environment.

Federal Oversight

The United States Environmental Protection Agency (EPA) is one of several United States agencies involved in the regulation of biotechnology products as part of a coordinated federal effort. During the past several years, EPA has been developing the specifics of its regulatory approach to these products. In order to put EPA's approach into perspective, it is helpful to have an overview of the federal concept encompassed within a coordinated federal effort. In 1984, recognizing its responsibility to address issues raised by the use of biotechnology, the United States government formed an interagency working group under the White House Cabinet Council on Natural Resources and the Environment. This group examined existing laws and concluded that for the most part, these laws would adequately address regulatory needs for biotechnology. A regulatory matrix describing applicable laws and responsible agencies was published in the Federal Register on November 14, 1985 (50 Fed. Reg. 47174).

Subsequently, the "Coordinated Framework for Regulation of Biotechnology" was published on June 26, 1986 (51 Fed. Reg. 23302). As used in the Coordinated Framework, the term biotechnology is broadly defined as "the application of biological systems and organisms to technical and industrial processes" (see "Proposal for a Coordinated Framework for Regulation of Biotechnology," 49 Fed. Reg. 50856, December 31, 1984). The Coordinated Framework spells out the basic federal philosophy for regulating products of biotechnology, details the network of agency jurisdiction over both research and commercial products, and includes statements of regulatory policy from the agencies principally responsible for such regulation. The United States approach to regulating biotechnology is based on the recognition that biotechnology encompasses a large and varied collection of techniques and activities, and that the potential products resulting from this technology will cover a wide spectrum of uses. The Coordinated Framework provides that biotechnology products will be regulated in the United States as are products of other technologies -- that is, by the various regulatory agencies on the basis of use. Thus, many agricultural uses of microorganisms, plants, and animals are regulated by the Department of Agriculture; foods and drugs are regulated by the Food and Drug Administration; microorganisms used as pesticides are regulated by EPA under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), 7 U.S.C. §136 et seq.; and commercial uses of microorganisms not covered by other existing authorities are regulated by EPA under the Toxic Substances Control Act (TSCA), 15 U.S.C.

§2601 et seq. Examples of uses covered by TSCA include microorganisms used in metal mining, degrading wastes, conversion of biomass for energy, production of proteins and enzymes for non-pharmaceutical purposes, and non-pesticidal agricultural applications such as nitrogen fixation.

EPA Statutory Authority

As indicated above, an essential characteristic of any regulatory scheme for biotechnology is that it promotes public confidence that the oversight process will protect human health and the environment. Similarly, the scientific and regulated communities must believe that the process is credible, equitable, and sound. At the same time, it is important that the development and commercialization of biotechnology products be allowed to proceed in a reasonable and timely manner. Accordingly, EPA's goals in developing a regulatory scheme for products of biotechnology are to (l) protect human health and the environment; (2) meet the public's need to be assured that use of living products does not present unacceptable risk; (3) expedite the regulatory process; (4) maintain flexibility in order to respond to rapidly developing knowledge and technology; and (5) to accomplish this end without stifling innovation and the development of valuable new products.

At this time, EPA's regulatory effort involving these products is, in large part, pursuant to its authority under FIFRA and TSCA. FIFRA creates a statutory framework under which EPA, through a registration process, regulates the development, sale, distribution, and use of pesticides, regardless of how these pesticides are made or their mode of action. FIFRA, therefore, covers natural and genetically altered microbes that are used for pesticide purposes. EPA has routinely reviewed and registered natural microbial pesticides, such as *Bacillus thuringiensis*, for years.

A pesticide can be registered for use only if the pesticide will not cause unreasonable adverse effects to humans or the environment. The "unreasonable adverse effects" test involves a weighing of the risks and benefits of use of the pesticide. In order to demonstrate that a pesticide will not cause unreasonable adverse effects, an applicant seeking to register the product must submit or cite data on subjects such as product composition, toxicity, environmental fate, and effects on nontarget organisms.

Some of the information needed to support registration must be developed under actual field conditions, and such preregistration field testing is authorized under FIFRA through the experimental use permit process. The results of such early testing are a critical element in determining when and under what circumstances a full registration may be issued.

TSCA gives EPA jurisdiction over the manufacturing, processing, importation, distribution, use, and disposal of all chemicals in commerce (or intended for entry into commerce) that are not specifically covered by other regulatory authorities (e.g. substances other than foods, drugs, cosmetics, and pesticides). TSCA authorizes EPA, through a screening process, to acquire information on chemical substances and mixtures of chemical substances in order to identify and regulate potential hazards and substantial exposures. Under TSCA, EPA can require testing of any chemical substance that may present an unreasonable risk to human health or the environment or which is produced in substantial quantities and may result in substantial environmental release or substantial human exposure.

TSCA's applicability to that regulation of microbial biotechnology products is based on the interpretation that living organisms are chemical substances under TSCA -- an interpretation that was embodied in the development of the initial chemical inventory in 1979. The basis for this interpretation is that all substances, living and nonliving, have a chemical foundation at the most fundamental molecular level. As a result of this interpretation, microorganisms (except for those in excluded use categories) are subject to all provisions of TSCA.

The premanufacturing notice (PMN) process implements TSCA's goal of screening new substances before they enter commerce in order to identify those that pose potential hazards. Manufacturers and importers of "new" chemical substances are required to submit data and other information to EPA that will allow the Agency to evaluate the potential risks of the product. If a potentially unreasonable risk is identified during the PMN screening process, EPA is authorized to achieve the appropriate level of oversight for the commercialization of the affected product.

Focus of EPA's Regulation

Through its statement in the Coordinated Framework, EPA made certain provisions immediately effective and indicated that rulemaking would be required before other provisions could be formally implemented. Where provisions were not immediately effective, EPA invited voluntary compliance in the interim.

Because microorganisms introduced into the environment have the ability to replicate, increase in number, and disseminate from the test site and disseminate themselves, EPA feels that it is prudent to address certain questions before some of these microorganisms are released to the environment. Accordingly, EPA's regulatory approach encompasses procedures designed to provide sufficient oversight of the initial products of biotechnology. In its section of the Coordinated Framework, EPA indicated that, under FIFRA and TSCA, it intended to focus regulatory emphasis on three categories of microorganisms:

1. microorganisms with "new" characteristics or that are new to the environment in which they are intended to be used (and whose behavior is therefore less predictable);

2. microorganisms that have hazardous components or characteristics (and therefore a recognized potential to cause adverse effects in other organisms); and

3. microorganisms that are used in the environment (and therefore have the potential for widespread exposure).

One of the most challenging issues for the EPA biotechnology rulemaking process has been identification of the scope of organisms to be subject to regulatory oversight. Because this is a cross-cutting issue for all the agencies included in the Coordinated Framework, development of a "scope definition" was undertaken as a joint effort. The result of this effort, "Principles for Federal Oversight of Biotechnology: Planned Introduction Into the Environment of Organisms With Modified Hereditary Traits," was published on July 31, 1990, and serves as guidance for EPA and the other agencies during their rulemaking processes.

In developing the Principles for Scope, the agencies relied upon "familiarity" as the basis for determining whether oversight is appropriate, and emphasized the role of information in the determination of "familiarity." (The appropriateness of using familiarity based on solid information as the basis for a flexible regulatory process is clearly supported by the 1989 National Academy of Sciences report, "Field Testing Genetically Modified Organisms.") Specifically, the Principles for Scope set forth the general directive that "[to] the extent permitted by law, planned introductions into the environment of organisms with deliberately modified hereditary traits should not be subject to oversight . . . unless information concerning the risk posed by the introduction indicates that oversight is necessary. Also included are examples of organisms that would "generally be excluded from oversight because their introduction is considered to be similar to previous safe introductions, or because other information available regarding the risk posed by such introductions (including knowledge that existing practices or regulations adequately address possible risk posed by the introduction) makes oversight unnecessary."

With the Principles of Scope as guidance, and utilizing provisions available under both TSCA and FIFRA that allow for flexibility in the regulatory process, EPA is well on its way to establishing the regulatory program promised in the Coordinated Framework. The Agency is currently nearing completion of the drafting process for its biotechnology regulations under both TSCA and FIFRA, and it is anticipated that the proposed rules will be published for comment in the near future.

EPA Review Process and Experience

Since 1984, EPA has reviewed a number of small-scale tests involving products of biotechnology, many of which were introduced to the environment. A scientific review process for such tests has been developed that EPA believes is credible, sound, and respected by the scientific community and which allows the public to feel confident that potential human or environmental impacts have been addressed. To date, the review procedures, which are briefly described below, have involved case-by-case evaluation.

When a submission for small-scale testing is received, TSCA or FIFRA staff groups evaluate the submission and develop a coordinated scientific position. During this process, hazard and exposure are addressed, potential problems, issues, or significant unanswered questions are identified, and the likelihood of significant risk from the proposed test is assessed.

Under both TSCA and FIFRA, intra-agency workgroups then comment on the positions developed by staff. If appropriate, the submission and EPA's scientific position are sent to other federal agencies for comment. Appropriate state regulatory agencies are also contacted in order to alert them to the submission, to discuss EPA's assessment, and to ensure that the federal and state positions are as consistent as possible. For some submissions, visits to the test sites are conducted in order to evaluate actual field conditions.

In order to obtain an independent peer review of EPA's scientific position, to address specific scientific questions raised by staff, or to identify any additional data that may be needed to complete the risk assessment, the submission and the EPA's scientific evaluation may be sent to a group of independent scientists. EPA has established a specific advisory committee, the Biotechnology Science Advisory Committee (BSAC) that it utilizes along with the FIFRA Scientific Advisory Panel (SAP) for these independent peer reviews. Several proposed field trials have been reviewed by specially convened BSAC, SAP, or joint BSAC/SAP subcommittees, and these groups have consistently endorsed the EPA assessments.

Public comment is considered an important aspect of the reviews, and for many proposals the public is provided several opportunities to comment during the review process.

In some cases, microorganisms that are subject to TSCA or FIFRA are also subject to the Federal Plant Pest Act or other statutes administered by the Animal and Plant Health Inspection Service (APHIS) or the United States Department of Agriculture. In such situations, APHIS and EPA conduct coordinated reviews. The two agencies cooperate closely, alerting each other to submissions, and sharing expertise and information. This close cooperation benefits both submitters and the agencies.

At the conclusion of a review, EPA determines whether the microorganisms may be released into the environment. Under both TSCA and FIFRA, this decision is based on an assessment of both the potential risks and the potential benefits of the proposed use of the microorganisms. Should the analysis indicate that use of the microorganism may pose unreasonable risk, EPA has authority under either statute to impose restrictions on its use.

Between the two programs, TSCA and FIFRA, EPA has reviewed approximately 75 submissions, some of which have been "second-generation" variations of previously approved

tests. While it is still too early to speak in general terms or draw definitive conclusions about the reviews, certain observations can be made:

1. EPA's review process has been effective in identifying and addressing risk concerns.

2. Evaluation of the proposed tests often requires different types of background studies, data bases, and scientific expertise than are required for review of traditional chemical products. Similarly, monitoring for living microorganisms once they have been released to the environment is frequently more complicated.

3. The issues giving rise to the greatest concerns are often not related to whether the microorganism performs its intended function, but rather to other, nonintended impacts that might occur.

4. Many (if not most) of the risk concerns about these microorganisms have been related to their potential impacts on the environment and nonhuman, nontarget species; to date, potential impacts on human health have not been a significant concern.

5. Monitoring data from some of the tests have confirmed that under actual use conditions, physical containment of the test microorganisms may not be feasible or possible. Accordingly, issues related to spread of the test organisms from the test site are appropriately considered in most risk assessments.

6. The small-scale tests reviewed thus far have been found to pose no significant risks. However, large-scale or commercial use of some of these microorganisms may raise more significant concerns, particularly regarding environmental and ecological impacts, than those addressed for small-scale tests.

As to nonscientific observations, it has become increasingly clear that public involvement is an important element of most test programs involving environmental release. Without such involvement, public fear of the unknown could derail the whole process and prolong the testing through extensive administrative and judicial maneuvers. The impact of such administrative and judicial activity can be seen by contrasting the first and a more recent EUP review of two genetically engineered microbial pesticides. In the first, the time elapsed between receipt of the EUP application and the test was almost two years. In between were two lawsuits brought in federal and state courts to stop the test, and numerous state and local administrative proceedings. The more recent EUP application, submitted after more extensive preliminary public outreach and presumably after the public had gained more confidence in EPA's review process, moved from submission to field test in approximately five months. There were no lawsuits or supplemental administrative proceedings involved with this review. It appears that the more the public knows and feels a part of and comfortable with the process, the less likely it is to obstruct the test. Hence, many submitters have elected to shield from public scrutiny only the barest essentials about their microorganisms and proposed tests.

EPA is using the experience gained from its early test reviews, along with public comments and advice from our BSAC, in fashioning its proposed regulations. Based on these sources, EPA has bolstered confidence that its basic approach, as set out in the Coordinated Framework and procedures developed for individual test reviews, are adequate to accomplish the goals for its biotechnology regulatory program. Therefore, in many areas, EPA's

proposed regulations are envisioned in much the same light as its policy statement in the Coordinated Framework.

To summarize, EPA's experiences over the last few years with the approach for regulating products of biotechnology first articulated in 1984 and later included in the 1986 Coordinated Framework, demonstrate that the process has met its major goals:

- utilization of a systematic approach for identifying and assessing potential human or environmental risks;
- incorporation of a peer review mechanism that draws upon independent scientists expert in diverse areas of relevant knowledge;
- establishment of an open process that allows for and invites public participation; and
- approval of field tests, the results of which confirm EPA's original judgment of insignificant risk.

Notwithstanding these successes, EPA recognizes that certain modifications to the current process are probably appropriate in order to accommodate in a timely manner the number of tests anticipated for review in the future. EPA is currently developing proposed regulations that will implement its modified approach. However, based on its past experiences, EPA is confident that its ultimate regulatory program will protect the public health and the environment from unreasonable risks while allowing the public to reap the benefits of scientific and technological innovations.

Keith Bailey, Chairman: -- We'll take this opportunity to have perhaps one question from the floor.

Seidler: -- In the exclusion by transduction, transformation, and conjugation are the organisms also excluded even if they are intergeneric products of gene transfer?

Zeph: -- As long as it is a natural process and hasn't been forced, say through the use of rDNA or alteration of the membrane, treatments that would force transformation, it would be excluded regardless of the source of the DNA.

Seidler: -- Would...electroporation be excluded?

Zeph: -- No. The definition includes the term 'physiological process.' This would prevent exclusion of electroporation.

Bailey: -- Thank you very much. No more questions?

AN ENVIRONMENTALIST'S PERSPECTIVE

Paul Muldoon
Canadian Institute for Environmental Law and Policy, and
Pollution Probe

Introduction

Good morning. The presentation that I would like to give today is something a little bit different than we've heard this morning. I'm from a legal background and I deal with a number of environmental groups. I hope what I have to say represents the public policy aspects of some of the tasks, some of the challenges, and some of the obligations that you will have to deal with in the near future. I should mention that I would like to narrow my discussion to open environmental releases versus contained releases. And I think basically what we are talking about at this point relates to genetically altered organisms, rather than naturally occurring ones. I would like to talk about two themes: one is, what is the role of the public in regulatory development such as the regulation before you, and second, what are some ideas, or what are some solutions, what are some inroads we could make in offsetting some of the concerns which the public has raised, and will raise in the future.

A number of my concerns relate not only to this particular regulation but to the inherent problems of the Canadian Environmental Protection Act itself. We were involved in the development of that regulation well before '86 when the first consultative process on it came out and I think we are now seeing some of the fruit of our concerns then. Unfortunately I think it's proven our view correct.

It is worth noting that in 1984 the Canadian Institute for Environmental Law and Policy held a conference on biotechnology and in that conference we brought in speakers from industry, the academic community, environmental groups, and other interested members of the public. One of the most interesting conclusions from that conference is very much relevant today. That conclusion was that the industrial community does not oppose the regulation of biotechnology so long as the rules are certain, predictable and applied in a manner that is fair-handed. Unfortunately, the way a biotechnology regime is developing in Canada it will be anything but predictable, anything but consistent, and unfortunately very piecemeal. And I think that those concerns are not only of industry but of the public also.

Role of the Public

What is the role of the public, and why should the public be concerned about this? And why should you be concerned? I think there are three general policy reasons why the public should be concerned. One is what I think is the obvious one. While the public may share in some of the benefits of biotechnology, they may also bear many of the risks. If they do bear these risks, they should have the right to participate in important decisions pertaining to the notification, assessment and release of biotechnology products. In making those decisions, agencies must decide in the "public interest." But how can they understand what the public interest is without the public there to give their views? Without fair, effective, and meaningful public participation from all the affected interests, such decisions are simply not "legitimate." The public has just as much stake in the process as the regulated community. Unfortunately, the public is often without resources for such participation. Perhaps that is

why the audience here today is dramatically under-represented from environmental groups and the public at large. The third general policy reason for having the public involved is that there will be better, more informed decisions made. While the public may not always have the technical expertise, they may bring a common sense approach to a very complex area -- something called the "wisdom of the public." It is in the realm of toxic chemicals that the regulated community and the regulators are finally realizing that the public approach to regulation of toxic chemicals is an approach that is feasible. And that approach is pollution prevention. The notion that one should put the vast majority of their resources to try and prevent the creation and use and generation of toxic chemicals rather than trying to control the releases and determining which is the acceptable release. That did not come from the regulators, it came from the wisdom of the public.

If you do then accept that there should be some sort of meaningful role of the public in this then why isn't the public here and why haven't you heard a lot about the public concerns? I have basically three reasons. One is that their interest in this field has not been nurtured. And for that I'm afraid we have to take mutual responsibility. But you have to take certain responsibility for providing the resources, providing the forums, providing the opportunities for the public to get interested, to get knowledgeable, and then have a route to effectively participate in these sort of processes.

The second reason is that it is a very piecemeal type of regulatory regime which is being created which causes confusion in the public -- both in the regulated and in the general public. The proposed regulation under discussion will contribute to this piecemeal regulatory framework. If a member of the public wants to investigate a particular biotechnology product, that person will have to go from department to department to understand the present status of the product. Moreover, it is simply an unknown as to how to have one's view heard. Another area of confusion of course, is that we are talking about a federal regulatory regime. A number of provinces are now struggling to figure out what the provincial regime should be. How can a member of the public possibly understand who has what jurisdiction, under what consideration, and what are the regulatory gaps?

And finally, there was also another regulatory signal sent out in December when the federal government released the Green Plan. The Green Plan stated that there are risks of biotechnology and that those risks necessitate a comprehensive regulatory regime within five years. Well, where does this regulation fit into this comprehensive regulatory regime? Is this it; is there more? As a member of the public where should I devote my scarce resources in providing input into your industry? Should we do it now or should we wait around to three years from now? I think the public demands, and this industry deserves, a comprehensive regulatory strategy, more coordinated, more integrated, and more importantly one that does capture the interest and participation of members of the public. It is not doing that.

The Proposed Regulation

The general comments with respect to public participation generally are particularly applicable to the regulation under consideration. Marshal McLuhan once said that the "message is the medium." When it comes to environmental decision-making, the process is the message. Hence, when reviewing the proposed regulation, it is necessary to ask: how open is the process? The response to this question will reveal whether this regulation will result in decisions which are fair to those involved, more informed and reasoned, and simply more legitimate decisions.

The regulation which is being proposed has a number of problems with it in terms of the public. And I look at these things in three ways. One is, to what extent does the public have access to the information being sought by the government? Does it have access to that

information and can it challenge the adequacy of that information upon which an assessment has to be made? Second of all, in terms of notification, what kind of notification does the public have in terms of new products? More importantly, what kind of notification does the public have in terms of field tests? What is the opportunity for the public to comment on the assessment, or on the information for the assessment, or on the field test decisions? I'm talking about just the right to comment, the right to make a submission. On the assumption that before you have the right to comment you have the right to know that there is a decision being made somewhere. Those issues are not in the regulation. Those issues are not in CEPA even though there is an opportunity to challenge the decisions under Sections 48 and 89.

Why am I so very enthused about getting people involved in that front end process? The reason is this; once the public catches on to the kind of risks involved, real or perceived, the areas where CEPA will allow them to participate and challenge it, is at the end part of the process. Hence, ironically, while one may believe that the process is quicker to exclude the public during the early decision-making processes, it must be recalled that the public can challenge decisions at the end of the process. Hence, if excluded, one can expect that there will be challenges late in the process since that will be the first legitimate opportunity for them to have their concerns expressed, evidence tested, and a number of questions answered. This is the kind of problem that I see if this regulation excludes the public. You are doing a disservice to the public but you are doing a disservice to the industry also. There are a number of ways to get around this. apart from very complex systems. I'll give you a few of them and I'm not adhering to any of them at this point. One of them may be a registry in terms of new products. There are many ways of giving the public notice other than the newspaper advertisements. That may be one way and may be needed in certain instances: registries and mailing lists.

I think more fundamentally that when you deal with the public there must be some sort of institutional coordination between the public, industry, and the government. In that context there are solutions which may be possible. For instance, some sort of information data bank and clearing house which would act as a liaison between what is being submitted, what the field tests are, where they are, and providing this as a conduit for public opinion and public information.

Now I'd like to get back to that in just a minute, but before I do that there is another general question about the regulation itself. It leads back to the notion of confusion of the public as to where this regulation fits into what the Green Plan said, in terms of what the provinces are doing, and in terms of the whole host of other regulatory initiatives that are out there. And again, I want to reiterate, environmental groups take some responsibility in trying to educate the public, but it is not their sole responsibility. You owe the duty to the public to inform them of your activities. And if you talk to some of the regulated industries now throughout the world, that's what's happening. It is better to face the challenges the public presents to you before, than after.

One of the questions that I have of a generic nature is what are the specific policy objectives of these regulations? What do you want from them? It is not stated. I suggest that this might be an interesting debate, but they must be stated. The reason I think they must be stated is because they would determine, from a public policy perspective, what the criteria is for assessment. If the policy objective is to promote biotechnology at any cost, that should be stated. As you might guess, I would not agree with that, but at least those kinds of implicit notions are up front. Because, no matter what interests one, as in all environmental decisions, there has to be some sort of decision to look at the societal impacts and benefits, and the environmental impacts and benefits. Unfortunately the societal impacts have traditionally been the winner in terms of socio-economic interests. It seems to me by looking at the Green Plan, and looking at the general weight of regulatory initiatives coming forward,

there is a need to look at the supremacies, the paramounts even, of environmental considerations and make decisions on the side of caution. I'll come back to that point. The point I want to make though is, to look at what are the policy objectives of this regulation. It would seem to me that the policy objectives of this regulation may not be the same policy objectives as toxic chemicals generally. Let me give you one example. Under the Green Plan it states that for persistent toxic chemicals the goal shall be virtual elimination; virtual elimination of the discharge of persistent toxic chemicals. Canada and the United States has an agreement governing persistent toxic chemicals in the Great Lakes which goes further in a way, or at least it can be interpreted as zero discharge. How does that interrelate with the type of regulatory system being set up here as the years go on and this area becomes more interesting to the public?

Let me just get back to a few other issues. I have three other issues, one of which deals again with public decision making or environment decision making involving the public, and that's the data base. There is a huge amount of information going to be generated by this regulation. It is going to be generated federally, it is going to be generated internationally, and each province is going to have to deal with the same information. In 1984 at the conference I mentioned, what was proposed was a national biotechnology information data bank. I don't think it has gone anywhere but the comment is still appropriate. Again you are going to hear, over and over, that there are some sixty thousand chemicals in commercial use in North America. Most of those chemicals do not have the toxicological profile necessary to make a rational environmental decision. That, in the public eye, is unacceptable. Any regulatory initiative which will land us back in that situation ten years from now will be deemed unacceptable, I trust. The data banks, I think, should go much further. If one would ask in Canada, what quantities of toxic chemicals are entering the environment, we do not know from Canadian sources. Other countries do know. In the United States for instance, the toxic release inventory states that there is 6.8 billion pounds of toxic chemicals entering the U.S. environment from certain categories of point source discharges. In Canada we have no national inventory like that. The Green Plan states, and hints at the need for, and commits to look at it. If this regulation is going to be proactive and avoid some of the problems which arose with respect to toxic chemicals, it must at least provide a sound data base for the biotechnology industrial activity.

Another concern is the environmental criteria for assessment. By and large, the focus thus far has been on toxicity. However, certainly it is necessary to examine issues beyond toxicity, including the broader questions of genetic diversity, ecosystem integrity, cumulative impacts and those more pervasive concepts which cannot be neatly packaged and examined under a microscope. What is the methodology and protocols for examining these kind of concerns? If one were to ask this, one could say well, we have a regulatory regime that is going to look at each biotechnological product individually. How does that react with the thousands of potential new products going to be released and how does that affect this whole notion of biodiversity, cumulative impacts, and all those sorts of questions that are very hard to assess? How is it going to address that? Again, if you can't answer that to the degree which satisfies the public, they will be relentless in their quests for responses.

The other question deals with liability and insurance regimes. As I mentioned before, one of the roles of having the public involved is because they do bear the risk. But what happens if something does go wrong? Should the public have to bear all the risks? What safeguards can be put in place to protect innocent parties? In this regard, a common suggestion is that there should be mandatory liability regimes in place before the release of any genetically altered organism. Unfortunately, this is an area that the provinces have not dealt with in any detail. From a legal point of view, there are some good arguments to suggest that existing liability regimes and the general principles of tort liability are simply inadequate to deal with the kind of problems arising from accidental releases or releases that cause unforseen environmental harm. If something does go wrong it is a lawyer's dream and an environmental

nightmare. There are many ways to do this....everything from a government fund, much like the spills one in Ontario where there is a fund which will compensate clean up, order clean up, and then the legalities are dealt with after. There is a whole range of options. I think that it is fair to say that these liability questions will probably be in the first wave of concern. But I think we have to sort of back up once again and say, where does all this fit in? What is the role of the public? Where is the information? How accessible is it? What is the process that assures public input and education? Who has to prove what? The question of onus was raised this morning and once again the onus will be on the public, whether or not it is early in the process or late, to demonstrate harm, that something is toxic before it is regulated. You are going to have a huge backwave of concern on that only because it has never worked in the toxic's world and certainly that flies in the face of a preventative regime which seems to be so crucial in the notion of sustainability. And last, this whole notion of liability, compensation, and how that will be taken into account.

Concluding coaments

The concerns raised are serious ones. The concerns raised can only partly be addressed in this regulation. But the concerns are very deep in the minds of the public. In fact, I would suggest that you already have heard groups, and I can mention a few, such as Friends of the Earth, that state we need a moratorium on the release of genetically altered organisms into the environment until we have some of these questions addressed. We need dramatic action, perhaps dramatic because of the level and degree of concern which we, as representatives of the public, hear from our respective peers.

Thank you very much.

Keith Bailey, Chairman: -- Thank you very much for a very provocative paper. I think we might have one or two question at this time.

Comeau: -- My question, and I probably have to elaborate a bit, is what do we do when we really know with scientific certainty that the public opinions are completely wrong? I'm going to put forward a provocative example. I don't know all the details or the story but you know quite well that some of the chemicals that Ben Johnson was taking were quite effective and legal, or non-legal, these chemicals are still around quite a bit. These are steroids, they have a very stable skeleton, they stay around and possibly get transformed a bit, and although diethylstilbestrol has been taken away there's quite a lot of those stories around. And I keep having nightmares that farmers somewhere in the world, I don't know where but I hope not in Canada, are giving the Ben Johnson treatment to their animals. I know that I've seen data on somatotropin research in which some proteins have been used to produce a similar effect. The difference being, that these proteins are highly degradable, and as far as I can see there is no risk to the public in consuming either the milk or meat coming from such treatments. Unfortunately the public has been hit so much by the DES story that it is not going to easily accept the other hormone that is much less harmful. Also, somatotropin, being a protein has the attractive possibility of being engineered in some organism. It is feasible to modify animals which would be more efficient in producing meat or milk. As you know, producing animal protein is environmentally very costly compared to producing a plant product. So, on environmental grounds, in my opinion, the use of such products as the hormones would be a sensible way to go. However, I know very well in the public eye, it's a dead issue.

Muldoon: -- Let me just reiterate what I said. I said that one of the reasons you want the public involved, it exactly addresses that point. It makes a legitimate decision because they've had their say, if they had the information, had resources, to test it. Don't underestimate the

public. The public are people like you or I, many of which have tremendous understanding in this area, and can make these kinds of tradeoffs. I don't ever underestimate the sophistication or the wisdom of the public in many of these instances. Secondly, you're going to be on a treadmill because you are always going to have suspicions because they are always excluded from the process. *Open up a process and they* will understand the side you are trying to get across and they will allow good decisions to go through. A good process usually leads to good decisions and bad processes inevitably lead to bad decisions.

Langer: -- I'd like to comment on the point which Paul (Muldoon) has just raised. Which is that how the public is not necessarily in the cheerleading section of biotechnology but neither are they against it. I think there is a realization that there are some real benefits for society and maybe a way to get out of some of the problems we are already in such as replacing toxic chemicals with less harmful products for agricultural applications for pest control. But that is going to have to be done within a regime where there is knowledge and when you are inviting environmentalists to a conference to represent, and I am speaking for Friends of the Earth, maybe ten organizations in this country have staff which knows anything about the issue. That does not match up to the level of effort that is going on within the industrial and government sector. This is something that is not clearly understood. I am pointing this out as a point of information so that you know when you are talking about 'the public' and who you've consulted just who's out there. The point is that people will be scared on the surface if they don't get more information. The onus is on the regulators and industry to prove and to educate so that they can win the confidence of the public. Not to expect the public to come rushing forward clapping hands because of a new biotechnology product.

Cummins: -- I have read, written, and distributed what I believe to be, certainly my perception, my experience in this area. Effectively there has been a conspiracy of silence on the part of the press in dealing with the release of these genetically modified organisms. I've often wondered if this is really an honest political conspiracy of silence or if it's just a conspiracy of dumb people not educating themselves. At any rate, my experiences have been 1) that the public is totally unaware of these releases because the press has not been able to cope with the releases, and 2) the information coming from the Minister's Office is technical gobbly-gook, frequently ludicrous technical gobbly-gook. In a release using CAMV, GUS, or CAT, in the corn which is a commonly practised and done in an indiscriminate and careless way, they use a promoter from CAMV which is a retrovirus, closely related to hepatitis B and for that matter to HIV. The response to this from the Minister's Office was that they didn't believe that promoter activity had anything to do with the virulence of a retrovirus. The promoter is the machine driving the replication in a retrovirus so essentially the only thing I could make from the Minister's comment, or that of the advisers to the Minister, was that they were either ludicrously off-base or were simply not aware of the significance of the retrovirus in this matter. In other words, the Minister was saying that the promoter activity in a retrovirus, and the CAMV promoter is one of the strongest retrovirus promoters known, is not significant. The press was poorly educated in this area, ignoring it simply because the word coming down from the ministry is technical gobblygook, and frequently very disparaging of the critics of the process.

Bailey: -- Thank you. Technical gobblygook is a real problem we all face and certainly there is also a lot of public and press gobblygook.

INDUSTRY PERSPECTIVE ON THE PROPOSED NOTIFICATION REGULATIONS ON BIOTECHNOLOGY PRODUCTS UNDER THE CANADIAN ENVIRONMENTAL PROTECTION ACT

Rob Quinn
President, Industrial Biotechnology Association of Canada

Good morning Mr. Chairman, ladies and gentlemen. I would like to thank the organizers of the conference for their kind invitation to speak at this plenary session and present the thoughts and interests, in effect, the perspectives of the Canadian biotechnology industry and the environmental regulation of products of this biotechnology.

My remarks will pertain to the following topics: first, a little background on the Industrial Biotechnology Association; second, our basic intention or attitude towards regulation; third, an outline of basic concerns with the proposed regulations, with the focus on policy issues. Then I will conclude with suggestions on how we should proceed to develop and implement regulations that truly serve and accurately reflect the public interest.

IBAC Background

The Industrial Biotechnology Association of Canada is but a few years old. Last year at this time the membershlp was 16 corporate organizations; we now number 30 corporate members.

lt is no secret to this group that industrial biotechnology is as old as breweries, wineries, distilleries, and bakeries. However, it is the new biotechnology that brought about the need to establish IBAC. While modern biotechnology is found in major and well established industries such as health, agriculture, food, forestry, fisheries, mining, environmental protection, and waste management throughout the world, we find trade associations dedicated to modern biotechnology coming into being over the last several years. Each of these associations seeks to serve and represent the common interests of companies, found in diverse industry sectors, that arise from their involvement in modern biotechnology.

IBAC is the Canadian association. One of our key functions is to represent industry concerns to governnment and to the public. Sound, domestically consistent government policy and legislation and internationally harmonized regulation obviously follows as a major, ongoing objective. Like the scientist entrepreneurs of modern biotechnology, we are pioneers endeavouring to be creative and innovative in seeking to serve the interests of our industry and, equally important, the interests of our industry's consumers, the general public.

Canadian Institute of Biotechnology

Part of this activity is the Canadian Institute of Biotechnology, which is a program operated by IBAC with strong financial support from Industry Science and Technology Canada. We are currently developing a new business plan for CIB so I will not go farther with this subject.

CEPA Regulation and Communication

Like all of you assembled here today, we've worked hard since the CEPA regs were released in mid-October to analyse them and to put together constructive comments, a lot of it criticism, and submit them by December 14, 1990. In many cases, we in industry exchanged briefs and the commonality of views is remarkable, especially on key issues. In other cases, there has not been such an exchange and, practically speaking, little opportunity to do so. To help, I have brought a limited number of copies of IBAC's brief and response to CEPA regulations. If none remain, please write "CEPA Brief" on your business card, give it to me and my assistant will be pleased to mail one to you.

In the meantime, one of the important objectives of this workshop is to learn about each other's views. So the remainder of my talk should, I believe, concentrate on providing a good overview of industry concerns.

Fundamental Premise

What is the fundamental intention or premise of Canadian biotechnology, be it traditional or modern? It is no more and no less than to create products that will confer substantial benefits for society. That has to be the starting point because otherwise the enterprise will simply fail for lack of interest.

Having said that, we have to recognize that modern biotechnology requires a great degree of scientific creativity and competence. Canadian industrial biotechnology possesses those attributes in full measure. Thus the industry's objective in regulation arises from its concern to develop sound regulatory practice in the public interest that reflects the high standard of scientific professionalism required for success in internationally competitive industrial biotechnology.

At the same time, the modern world economy requires rigorously efficient administration in our enterprises if they are to succeed -- and that applies to government regulators as well. To succeed, Canadian biotechnology has to conquer world markets; the domestic market just is too small to sustain research, development, manufacturing, and production of many biotech products. But our Canadian market is just not big enough or rich enough to attract international biotech products.

The consequence for Canada is that Canadian regulation has to protect legitimate Canadian consumer and environmental interests and simultaneously foster internationally competitive Canadian biotechnology. That's no small challenge and to meet it we are going to have to recognize the need for industry and government representatives to work closely together. And that, by the way, means ongoing dialogue.

That's our starting point. Now let's turn to to the proposed regulations. We regret that we cannot say they are in good shape. We understand that there is some history to their development and some of us are aware of adverse political and administrative realities, which frankly discouraged a genuinely collaborative and consultative approach in the complete public interest. Let's put that behind us and insist that we find a better way.

The first step is to spell out clearly what's on all our minds. Having said that, here are our concerns with the draft before us:

1. Too much information demanded. The present draft represents a set of exhaustive and costly information requirements increasing in relation to the level of production rather than the level of risk or potential harm to the environment.

In this connection the recently released version of the Green Plan refers to great benefits of biotechnology but also to significant risks. Why not list those risks and seek agreement on them in order to have a common understanding of the problems?

If the benefits of effective regulation are to be realized, the costs -- to industry and government -- must be realistic and not prohibitive domestically or vis-à-vis international competitive realities. Could Environment Canada really cope with all the information it wants? Will the Treasury Board provide those kind of resources?

2. **Too many products.** What do the proposed regulations encompass? The short answer is seemingly everything. The introductory memorandum to the proposed regulations arbitrarily declares all biotechnology products to be "new" products simply by refusal to compile a Domestic Substances List for biotechnology products already in common use and in most, if not all cases, not a problem. Rather, the approach is to require Canadian industry to absorb the unnecessary cost and effort of supplying "satisfactory evidence to substantiate that specific products were in commerce in Canada" sometime during 1984-1986 in order to get them onto a Domestic Substances List and hence exempt from these regulations.

This kind of approach will incur excessive investigative, monitoring, and enforcement costs for the government; i.e. for the poor general taxpayer. In addition, countries exporting such substances to Canada will complain that these new restrictive actions amount to non tariff trade barriers. Treasury Board will not like this approach at all, especially when the Act provides a much cheaper and better way!

We recommend that an inderdepartmental team get cracking on a DSL for biotechnology and circulate it for public comment. We will help to complete it.

3. **Too unfocussed.** The proposed regulations rely on monitoring the development process or exempting importation or manufacture of small quantities rather than environmental risk represented by the substance. We believe the issue is neither scale nor quantity of production but rather degree of risk, taking into account conferred benefits obtained through sensible, safe use. Moreover, when a new product or development process may conceivably be, or known to be of substantial risk, a sensible regulatory approach may be a licensing procedure, which avoids repeated applications.

So firstly we recommend that the level of production approach in these regulations be scrapped and replaced with a risk based approach. This in some ways may be analogous to management by exception. Government and industry really have no choice but to concentrate scarce resources only on those substances requiring careful handling by competent professionals -- that is -- good professional practice which, in effect, should be the goal of this exercise -- to establish what constitutes good, professional practice when dealing with potentially or known high risk substances vis-à-vis environmental concerns.

A second recommendation in this regard is this: when development, manufacturing, or application of the product has a known but relatively consistent high risk factor, a licensing approach, capable of international acceptance, may be the best and cheapest way to deal with the matter.

A third recommendation, to promote conservation and best utilization of scarce resources and existing expertise, arises from the fact that the Act states that products already regulated under other Acts of parliament will continue to be so regulated. So we recommend that the next draft clearly spell out those Acts and regulations and the kinds of substances, products, etc. Environment Canada expects to see regulated accordingly. That kind of approach will conserve resources to devote to your responsibilities and to avoid duplication by government and industry, not to overlook prevention of turf wars and so on.

4. Too domestic. The future of Canadian biotechnology depends substantially on success in world markets. Consequently there is a basic requirement for internationally harmonized regulations consistent with those practices and regulatory frameworks developed within institutions such as the Organisation for Economic Cooperation and Development.

In effect, Canadian regulations must be no more onerous than those of our major trading partners whose citizens are no less concerned for the environment than we. Indeed, being more demanding or onerous in no way guarantees greater public safety.

To help their respective governments arrive at sensible and effective regulations, American, European and Japanese industrial biotechnology scientists have been working on a set of scientific principles on which governments could base regulation of biotechnology products. Canadian representatives are going to join this group this spring to participate in this valuable work. IBAC will act as the conduit first to obtain Canadian industry endorsement views of this international committee's work and then to pass it to appropriate Canadian authorities.

I could continue with other concerns but it may be easier to read them in our brief and in many others, notably that of one of IBAC's outstanding members, the Toronto Biotechnology Initiative. In this connection, Eileen McMahon is to be saluted for pulling together and writing a splendid brief.

Conclusion

To sum up our concerns, these proposed regulations are just too much -- too much paper, too many products, too unfocussed and too domestic or to be frank, too parochial.

Obviously Environment Canada, and perhaps their colleagues from Health and Welfare Canada, have very different views on appropriate regulation than those who wish to develop and/or market biotech products which we all agree confer substantial benefits.

Consequently, we have to find a way to develop a common understanding of the facts of whatever problems there are and then an intelligent and practical approach to them. It seems a tall order to attempt to achieve that today and tomorrow. What seems required is a return to proven methods and in this case that would be the establishment of an Industry/Government Working Group.

This is a pioneering industry. Hence, modern biotechnology is going to require sensitive and innovative approaches to develop sound regulation in the public interest. Because it is so new, there are not all that many experts available. I suggest government and industry need to combine forces so we can do the job properly.

Thank you. Questions?

Langer: -- You mentioned that the Canadian Institute for Biotechnology is supported in part by the Department of Industry Science and Technology. In the context of the previous speaker (Muldoon) and some of the conversations we've had about public involvement, I'm wondering if that institute and your association would support an approach to Industry Science and Technology to provide financial assistance to a group of public citizens who are interested in learning more about biotechnology and having concrete and constructive input into the development of biotechnology regulations and procedures, for instance.

Quinn: -- Well I won't dare speak for ISTC but I happen to be a proponent of public participation and I've certainly been involved in it in other fields. I tend to agree with Paul

(Muldoon) that getting all the facts out is very wise but a question of how we might get involved with supporting a group is a complex one. It is a fledgling industry, as our Chairman has pointed out, and our resources are terribly limited. In principle what you are saying is attractive; in practise I don't know if I can do very much at this point.

Langer: -- What I'm saying is, from the Association's perspective, we would like to see if there would be support for approaching an area of government that seems intent on supporting the biotechnology industry development and which should have more attention on the public input area as well.

Quinn: -- Well let me put it to you this way. If you give me something that I can take to my board of directors, I'd be happy to present it to them.

Langer: -- The other thing I wanted to comment on...you mentioned that perhaps the best way to approach us now (the public) is for industry and government to put their heads together. I think you are missing an essential element in forgetting the previous speaker. I don't think industry and government alone are going to swing all of this at this point in time. There is the public sector to consider.

Quinn: -- I think you have a good point. What I was trying to get at was to bring together the science developers and the science regulators. They have to talk to each other a lot more than they have been. They've got to get together to define what their problems are and what is the best way to resolve them. In terms of public participation, and we are all members of the public -- we are not excluded by being scientists or by being in the business -- we all have to have the technical wherewithal to be able to contribute. This means doing a lot of homework, and being able to look at this and say what is the need, what is the issue, what is the problem, and what do we want to achieve? Its principle can be easy to enunciate but difficult to implement.

GENERAL DISCUSSION

Keith Bailey, Chairman: -- I see from the program that the next item is a general discussion of the papers that we have heard this far. However, before proceeding, I would like to ask our six speakers to the dais. At 12:15 Sheila Forsyth will provide the background information on the syndicates and get you on your way there.

So while the speakers are coming forward I would like you to mull over your choice of syndicate groups. The Scope of Regulations group appears to be oversubscribed and may have to be split, or perhaps some people have had second thoughts and would like to join one of the other groups. Keep it in the back of your mind until you hear what Sheila has to say.

Well, all speakers seem to have arrived on stage so the floor is now open.

McMahon: -- I am here today representing the Toronto Biotechnology Initiative. This is a group which represents approximately 90 members drawn from the biotechnology sector in the greater Toronto area. What I would like to mention is, that TBI wholly supports the comments made by Rob Quinn this morning on behalf of IBAC. In addition, I would like to make a few comments about TBI's concerns about the regulations.

My first point is, that Section 26.(3) of CEPA exempts from its regulations certain products that are already regulated by other federal departments. The wording of that section, however, has to be closely looked at. The products require notification prior to their manufacture, importation, or sale. That's the first requirement. And secondly, there is a requirement that the federal government assess toxicity. My concern is that diagnostics, for example, regulated under the Food and Drugs Act, do not require notification prior to their sale, in many instances. Furthermore, federal government departments often don't assess toxicity to the environment although they may assess toxicity to health. As a result it is not at all clear, in my view, that that section exempts from regulation those products that are already regulated by another department of the federal government.

The second point I would like to make is that we've heard a little this morning about the waiver provisions of CEPA. In other words, where information requirements are far too excessive or not required to assess toxicity; the Minister can waive the requirement for that information to be submitted. The waiver provisions in CEPA subsection 26.(4) are quite formal in that they require notice to be published in the Canada Gazette. As a result, TBI has concerns about the confidentiality of information. Competitors, for example, would have knowledge that an application was filed with Environment Canada and perhaps would also be tipped off to file an access to information request. We do have concerns in this regard with the waiver process. It appears far too formal and should be more flexible.

The third point also touches on confidential information. While CEPA does exempt certain information from access by the public, many types of information are subject to public disclosure. As the result, many members of TBI have expressed concern that, while protection is afforded by Consumer and Corporate Affairs for example, under the Patent Act similar protection is not given by Environment Canada. A consequence is that a person familiar with the "access to information" process could certainly glean information on the activities of their competitors.

The fourth point I would like to make is that Larry Zeph has mentioned the U.S. EPA will be putting forth some proposed regulations under TSCA, and my understanding is that these propose to restrict the scope of federal oversight. In other words, the U.S. government has learned that certain naturally occurring products and various other products are not toxic.

Regulations should be proportional to risk of toxicity. Many members of TBI recognize that certainly some products should be regulated and certainly regulations should be proportional to the risk of toxicity.

My last point is that TBI certainly supports public awareness of what is happening in the biotech industry and feels that the public is to gain from knowledge of biotech products and what they can do. However, an approach of regulating all biotechnology products would encourage the public's perception that all these products have a toxicity associated with them. This is simply not true and we would do some benefit to the public by first of all educating them, and secondly showing to the public that not all biotech products have risk of toxicity.

Smith: -- I would just like to address one thing. The issue has been raised several times about making regulations proportional to the risk. In the process that we are dealing with under the new substances part of CEPA, this is what we hope will be the case. When we get to the point of controlling a particular substance it will be based on a risk assessment. The format under the new substances part of CEPA is an opportunity to look at a certain amount of information in order to make that determination. The question I would put to all of the participants is, what should that information be? What do we need to look at to determine if an individual substance poses a risk or not? I guess the analogy might be in the way the new substances part of CEPA is being applied to chemicals. I think it is acknowledged that certain chemicals are toxic in the way toxic is defined under the Act, other chemicals are not. The whole process of going through this screening mechanism is to be able to identify those ones which cause the problem. I'm certainly more than happy to hear everybody's ideas about what this information should be, what we should be looking at in order to divide the products into those posing risk and those that don't. From the health assessment viewpoint we want to know the best method to integrate what we already know about microorganisms, a specific organism, and the test data.

Again I'll offer these as examples of the types of issues that we're wrestling with and where we would like your input.

McIntyre: -- I'd like to echo John's (Smith) concerns and gratitude as well for the quality of the overall response of the Toronto Biotechnology Initiative. The concerns they've expressed will certainly act as grist for our discussions later on this afternoon.

I think the point that you've raised on the overall comprehensiveness of the draft biotechnology regulations is a good one and I think in our on-going discussions which occur quite regularly with the other regulatory departments, it is certainly one that will be taken up.

The other interest I have at the moment is in getting some information from you, getting some dialogue from you, getting some recommendations from you in terms of the package that you see before you -- how the package can be modified and amended, as you see it.

Samagh: -- I would like to comment on Mr. Quinn's presentation. Have they put in their brief how the overlapping of the products and regulations should be handled and how they should be put into the CEPA regulations? Secondly, I would like to point out, as I'm sure you are aware, that there is an interdepartmental committee in the federal government that is looking at the harmonization of the regulations within the departments.

Quinn: -- I wasn't quite sure of your question. Did you ask whether we had set out a clarification on how that Section 26.(3) should be divided?

Samagh: -- Yes, and have you any suggestions on how this issue should be solved?

Quinn: -- I think we echoed what Terry (McIntyre) had said, or perhaps Terry is echoing us; I'm not sure whose turn it is to curtsey or bow. As far as we're concerned full advantage should be taken of Section 26.(3). Eileen (McMahon), who is a lawyer and I'm not, touched on the suggestion of ambiguity. As Terry said this morning, we should try to use existing regulatory frameworks, existing legislation, and I would agree with that thrust. I think the group should draft something soon that states, "this is what we think this means; this is how we are going to interpret it," and be very specific about it. We did not take that step directly and in detail in our brief because it is a major work in itself. But yes, this is the way we think it should go. Does that answer your question?

Walter: -- I'd like to address this to Terry McIntyre. I know you are very familiar with the policy objectives of CEPA and you may wish to take five minutes or so to discuss with the audience here just what Environment Canada's objectives are.

Bailey (Chairman): -- Two minutes please.

McIntyre: -- Well I'll take one of them and maybe John (Smith) would like to add. I don't think we have set down a specific policy objective. I can perhaps outline what I would think the philosophy behind the environmental component of the regulatory package. And what I am going to say is not in order of importance. We are looking at the development of a regulatory regime for biotechnology which is harmonious with regulations being developed elsewhere in the national and international arenas, regulations that are consistent in application, user friendly, sensitive to developing industries and not unduly dampening to Canadian entrepreneurial spirit, but unequivocal in their efforts to protect the environment and human health.

Muldoon: -- I would just like to mention one thing. Although they might be very sensitive to industry it's still exclusive of the public and I think this should be a policy objective. If you look at the development of the chemical industry versus the biotechnological industry I think we have a lot to learn. With the chemical industry we didn't do it well and one of the reasons was that the public was excluded. The air and water quality standards of this country were negotiated behind closed doors and there is a backlash against that. Here we have the opportunity to do it right and I think one of the first steps is recognizing public input as a policy objective.

McIntyre: -- When I mentioned that the unequivocal part was the protection of human health and the environment, I should have mentioned that we have a couple of internal mechanisms which we use to access and gauge or assess what the public perceptions are in this regard. We've had two very successful national public consultation sessions where biotechnology was put on the agenda. We got some very positive feedback from the public in attendance. One of the difficulties that we had was identifying the public in terms of distributing this last draft of the regulations. Subsequently we contacted the Canadian Environmental Network to give us a better appreciation in terms of, in their estimation, who the public was, ultimately to receive copies for review.

Kucey: -- One question I would like to put up to the whole panel. With respect to the public, I realize that when we see the word 'public' we tend to think of one large group, but in actual fact there are two groups there. There is the informed public, and there is an uninformed public. I would like to ask to what extent, although the concerns of both groups are very important, to what extent do we take the opinions of the two groups in the development of further action?

Quinn: -- That is a tough question. You've divided the public into two groups and I think you have to break the public out into many groups depending on their particular interest in a biotechnology product. We had one gentleman stand up earlier and talk about the problem

in waste treatment plants, and this is an area where the public is very active, and we are spending hundreds of millions of dollars in the improvement of these processes. Then we go to the area of health where something is being developed that, in simple language, aids a transplant. There will be another group of the public who will have concerns in this area. So it's not just a question of one group or another.

Kucey: -- I didn't mean to imply that only the one group is always informed.

Quinn: -- I agree. However, the public advocates, the individuals who read something and follow it up by attending meetings to learn more, are in the minority. The fact of the matter is, governments and people producing the products are the ones who are held responsible for the decisions and they have to be responsible decisions. At a certain stage in the activities they have to make a decision and live with it. In this regard, consultation with the public can be extremely useful when all the factors involved in the decision are laid out, and considered responses elicited.

Muldoon: -- I would agree that there is a plurality of interests. That is why I think you have to get back to the basic question of process. How do you accommodate the plurality? You are not going to get everyone agreed on every issue but I think it is fair to say that the notion of public consultation is more than just a one shot deal and saying, "Here, have your say." It's a matter of dialogue. It's a matter of a process with appropriate tools on both sides to carry on a system of interaction, an input, so that at the end of the day someone has to make a decision. Well fine, but at least you have an array of opinions based on informed dialogue. This is a process, it's not an end, and processes tend to take a little more time. But if it is a good process things will work. So, if the question is, why do we have an uninformed public, I think the answer is, there isn't a lot of literature, there isn't a lot of discussion, there isn't a lot of dialogue among the people of the public to really become informed of these issues. When they hear about a field test they get very worried and a huge amount of concern is expressed. That, to me, is in part because maybe there is a real risk there and two, maybe there isn't any information upon which to base a decision as to whether or not that risk is real.

Bailey: -- Thank you all very much. I would like to thank all of our speakers for their excellent presentations and also the organizers for putting together this interesting program. I will now turn you over to Dr. Sheila Forsyth who will lead us through the tasking of the syndicates.

TASKING OF SYNDICATES

Sheila Forsyth
Biotechnology Section
Commercial Chemicals Branch
Environment Canada

We've heard a summary of the opinions, the comments and the approaches of various sectors concerning the draft regulations and now it is your turn, when we go to the syndicates this afternoon, to put your points of view across in discussions amongst yourselves.

We've provided this opportunity for you to consult with each other and, as Rob Quinn has mentioned, to hear the opinions of other people who have provided us with briefs and comments. We hope that your ideas will coalesce and that you can provide us with comments and recommendations that we can take home and use in the drafting of the regulations. We know that with your help we can build a workable set of regulations that will do what they are supposed to do in the protection of the environment and safeguarding the health of Canadian citizens.

Your discussions this afternoon should focus on the regulatory requirements. We ask you to please try and stay within the confines of the draft regulations and not go off on tangents not associated with the regulatory process. This way we will be assured of concrete and pertinent comments that we can use to address the regulations.

If you examine the lists of the syndicate groups in the lobby, you will note that the "Scope of Regulations" has been oversubscribed. If some of you would like to reconsider, you may join one of the other syndicate groups. It may be that some of you have felt that the Scope syndicate is there to cover all aspects of the regulations, where in fact it is set up to deal with provisions for exemptions and exclusions, and how waiver provisions should be used. Given this, you may wish to transfer your allegiances.

The "Microbial Consortia" syndicate is there to discuss issues of identification of the organism, how you would deal with a group of organisms that are not necessarily identifiable individually but work together as a group, and the assessment periods.

The "Contained Use" syndicate will deal with research and development, commercial manufacture in a contained facility, and various other items that we would like you to consider in these particular areas.

The final two syndicates, namely "Environmental Data", and "Health Data" will, as their titles imply, deal with the data requirements in these two areas and I know that a number of you have very definite suggestions on how these should be restructured.

When you are in the syndicate rooms, I would ask that you select a secretary or a scribe to keep good notes of your discussions, preferably on flip charts so that they are always visible. Please retain all your records so that your discussions can be reflected in the Proceedings of the workshop. After you have elected or co-opted your scribe, we ask that you brainstorm the issues, some of which have been outlined in the "Possible Issues for Discussions in Syndicates" document. This document is simply a framework for your discussions and if you

find something outside of this that needs addressing, then do so. Once you have your list of issues pulled together, we suggest you prioritize them in the order you would like to discuss them, and then proceed.

At the end of the sessions today I would like all the syndicate facilitators to meet here in the theatre so we can discuss progress and any restructuring of the syndicates that may be necessary for tomorrow's sessions.

When we all meet here tomorrow morning it will be necessary to reassign rooms to the various syndicates and at that time I will give a brief overview of what progress has been made today. You are free to move around. Just because you have signed up for a particular syndicate does not mean you have to stay with it all of today and all of tomorrow.

The Environment Canada and Health and Welfare Canada people in attendance are here in a resource role only and are not present to discuss how they want to see things resolved. We are here simply to answer specific questions, and to explain, if necessary, why some things are written the way they are. We are here to listen and learn.

POSSIBLE ISSUES FOR DISCUSSIONS IN SYNDICATES

This list of issues is tendered to provide a focus and a starting point for discussions in the syndicates. The list should be used to stimulate discussion and to encourage development of solutions to key issues identified in the written comments to the regulations.

The list is not meant to be exclusive. Issues not listed here and which shoud be discussed should be brought to the attention of the facilitator for inclusion on the agenda.

Issues have been divided into the five areas mentioned on the confirmation form.

PROPOSED SYNDICATE	FACILITATOR
SCOPE OF REGULATIONS	Mary Mes-Hartree - Forintek
CONTAINED USE	Reg Kucey - Ag Canada
ENVIRONMENTAL DATA	Ray Seidler - US - EPA
HEALTH DATA	Earle Nestmann - CanTox
MICROBIAL CONSORTIA AND OTHER ISSUES	David Major - Beak Consultants

Suggested procedure for syndicates -

Identify issues to be discussed.

Prioritize issues for discussion.

Discuss solutions and recommendations.

Prepare report to plenary.

ISSUES

SCOPE OF REGULATIONS

Potential provisions for exemptions/exclusions and how they should be used:

- Domestic Substances List (DSL)
  - What should be listed?
  - How should it be listed?
- Schedule XVI (Use-specific exemption)
  - Criteria for inclusion
- Waiver provisions

CONTAINED USE

- Definition of contained facility
- Quantity trigger for exemption
- Biosafety Committees
  - Role of and membership
  - Reports
- Contingency plans
- Role of Good Industrial Large-Scale Practices (GILSP)

ENVIRONMENTAL DATA

- Tiering of data
- Use of and protocols for microcosms
- Monitoring - when and how
- Selection of nontarget substances
- Endpoints and protocols for measurement of basic biological, enviromental effects and fate data

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HEALTH DATA

Need for specific endpoints
- Hypersensitivity
- Irritation
- Toxicity
- Infectivity

Exposure estimates

Alternate testing strategies
- *in vivo*
- *in vitro*

MICROBIAL CONSORTIA AND OTHER ISSUES
(DEFINITIONS, IDENTIFICATION)

Microbial consortia
- Data requirements for identification, environmental and health effects

Other issues
- Assessment periods
- Identification - microorganisms, biochemical, additional terms that should be defined.

SUMMARY OF FIRST DAY SYNDICATE DISCUSSIONS

Sheila Forsyth: -- Good morning everyone. Before we move back into our syndicates I would like to try to quickly summarize what the various groups have covered up to this point. This will give you a chance to move around, if you wish, and me a chance to reassign some of the issues from group to group.

I also have a few requests from some of the syndicates for particular members to move into their groups.

Late yesterday afternoon we had a meeting of the facilitators, to outline the progress that has been made. I'll try to summarize this now and if there is something that I neglect to mention, please do not hesitate to speak up. The summary may give you some direction and help you decide where you should go this morning.

The syndicate on **Contained Use** has been working on definitions of contained facilities including contained production and contained use. They have discussed the quantity trigger - the 10 litre that is in the regulations, and they are looking at some form of a tiered system.

Contained use:

- definitions - contained facility, contained production, contained use
- quantity trigger
- biosafety committees
- GILSP

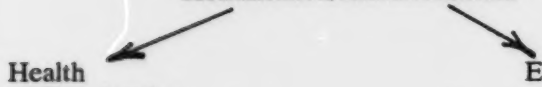
They have yet to discuss the role of biosafety committees and the role of the GILSP principles. What they plan to do is run through everything once and then go to the top and talk it through again. So, if anyone is interested in this area and wants to join them today, you still have the opportunity to comment. I know there are a couple of people who have just arrived today, and this is their area of interest.

In the **Microbial Consortia** syndicate they have discussed the approaches on how you would do a risk assessment of a consortia. They have talked about definitions and how you would identify a consortium, a single product, or a single species type product, and they are coming up with some recommendations there. They do have some ideas to hand off to two of the other syndicates. They would like the Health Data syndicate to consider the effects and testing of consortia; how you would approach a testing methodology for a microbial consortium, and the byproducts of the microorganisms. They would like the Environment syndicate to consider how they would carry out environmental effects testing and fate testing on contaminants, byproducts, and consortia.

Microbial Consortia

Consortia - risk assessment

Definitions
Identification/characterization



Health
- effects/testing of consortia and byproducts

Environmental
- environmental effects on contaminants, byproducts and consortia

Assessment Periods
- submission/data packaging
- data bases
- culture collection/protection of CBI

This syndicate is still planning to look at the assessment period and three other areas, including what a submission looks like, how to deal with a submission, when you should consider it complete, and what EC and HWC should do with it at that point. They are also looking at data bases, the culture collection issue and how to protect CBI (confidential business information) when putting something into a collection. If any of you are interested in these areas please join this group, or if you are already in one of these two syndicates you can start thinking about how to deal with these concerns.

In the **Environment** syndicate they have worked on a tiering matrix which they plan to present to us this afternoon. They have started to work on the question of microcosms, some of the protocols, and ideas on microcosm use for environmental testing.

Environment
- Tiering
- Microcosms
- Endpoints
- Selection of non-target substances

They have still to consider endpoints and the selection of non-target substances: how to select them, what numbers of substances, and what type of substances should be tested. They have a request for additional industry people to join them to make the group more complete.

The **Health Data** syndicate is working on the information requirements. Should they be in the regulations as they stand, or should the detail be part of the guidelines? They would like to maintain flexibility in the regulations to accommodate growth of the knowledge base that will take place. The question is whether this flexibility would be maintained if specifics are introduced into the regulations. They will present us with recommendations in this area this afternoon.

Health Data
- Information requirements - regulations vs. guidelines
- Flexibility
- Knowledge base
- Endpoints

They plan to move on to further detail on endpoints. The health group would also like to have additional industry people join them.

The large group that has been meeting in the theatre has had the monumental task of dealing with **Scope of Regulations**. They have taken some twenty-six issues and boiled them down to four major issues. These include the objectives of CEPA, the overlap or possible overlap with Acts of Agriculture or Health and Welfare, the role of the provinces, and how the provinces will be informed of what is going on under CEPA. They were also looking at the whole area of contained use and contained facilities and the role of CEPA in these areas. They will have some recommendations in this regard.

Scope of Regulations

1. Objectives
   - CEPA and other Acts
   - role of provinces
   - contained use - role of CEPA
2. GEM/NOM
3. DSL/Schedule XVI
4. Public information/input

Today they are moving into the area of genetically modified organisms vs. naturally occurring organisms and how we should be dealing with them under the regulations. They are also going to consider the DSL (Domestic Substances List) and Schedule XVI exemptions and approaches that can be used under CEPA. The final area is that of public information and how to provide the public with mechanisms for inputting to the system.

Do any of the syndicate leaders have anything to add to this summary? If not, we can return to our assigned rooms and reconvene here in the theatre this afternoon at 1:30.

SYNDICATE REPORTS AND DISCUSSIONS

Rob Quinn, Chairman -- Welcome back to the final session of our workshop. Before we proceed, I have been asked to advise those who took copies of the **BIO** TECH - A Users Guide to please sign the list on the registration desk to ensure you receive updates. Updates should be published in six months or a year, so be sure you sign for them.

This afternoon we will ask for the reports from the syndicate groups in the following order. We will start with the report from the Microbial Consortia syndicate followed by Health Data, Environmental Data, Contained Use and finally, Scope of Regulations. I'm hoping each group can hold their presentations to roughly 15 minutes so that we will have ample time for debate afterwards. Following the individual presentations I will take a question or two from the floor for clarification purposes. After all the reports have been heard we will open the floor to general questions.

I'll now ask David Major to start with the report on Microbial Consortia.

Report of SYNDICATE I

MICROBIAL CONSORTIA AND OTHER ISSUES

David Major, Facilitator
Larry Zeph, Secretary

Issues for discussion:

Microbial consortia
Data requirements for identification, environmental and health effects

Other issues
Assessment periods
Identification - level of detail required
definitions - microorganisms, biochemical, additional terms that should be defined

While essentially dealing with consortia, a lot of what we have to say applies to individual microorganisms either naturally occurring or genetically modified. I'd like to open with a general statement to the effect that we believe a tiered evaluation system should be employed, based on a case-by-case risk analysis approach which considers:

- the potential risk of the proposed use
- the scale of use
- availability of extant data on risk and identification of the microorganism
- resources required to identify to a specific level.

The identification and/or characterization of the microorganism is of utmost importance in that we have to have some means of recognizing organisms to enable us to monitor those released into the environment. Secondly, the more we know about the organism the better chance there is of evaluating its potential risk. There is no single approach that can be taken in the identification of a microorganism or used to describe a consortium of microorganisms. With individual or pure cultures of organisms, we suggest that they be classified to the genus level at least. A more precise identification may be desirable depending on the risk factors associated with the organism. Obviously, more information will be required if the risk is high.

We've tried to identify a number of specific endpoints that can be used for the identification but we cannot specify universal methodologies for the process. Endpoints we think would be useful include closeness to other known taxonomic groups. It is generally felt that familiarity with the known gives one a better chance of evaluating potential problems. Closeness to other functional groups might provide a biochemical approach to evaluation. Another endpoint would be the provision of an unique set of identifiers. For example, if you can't classify your pseudomonad to the species level, you might be able to say that it has a number of cultural, genetic, biochemical characteristics that are similar to *Pseudomonas*

putida. In this way you would have some point on which to hang your hat when you evaluate risk or identify an organism in the environment.

Specific methods we have discussed for identification include phospholipid fatty acid analysis (PLFA), recombinant RNA analysis (rRNA), DNA analysis, monoclonal antibodies (MAb), phage, and of course, the classical cultural and biochemical techniques.

Up until this point I've been basically discussing the single organism situation. Consortia pose a different set of problems. We had considerable discussion on whether or not we should be trying to identify all the individual species making up the consortium. We concluded that it is not necessary to identify each individual species in the mixed population. Rather, one should be able to describe the consortium in terms of overall characteristics. A minimum level of human/animal health data would be required depending on the presence/absence of pathogens. In the absence of precise identifications of individual species in the consortium, proponents could have difficulty in patenting. While not of direct concern to the regulators, it is something that you should keep in mind.

Returning to specific identifiers, we'd like to point out that PLFA, rRNA, and DNA analyses all have potential in the identification/characterization of consortia in addition to functional tests representing combined activities of the populations. These methods can be useful for tracking consortia after application. Sampling and analyses for PLFA and DNA could provide useful fingerprints for establishing persistence or fate. These methodologies have shown some promise but a great deal of research is still required in their development and application.

With both individual organisms and consortia we feel that the inability to provide information on the identification to a specific level (genus, species), could be compensated for by the provision of supplementary data on human health and environmental effects.

From our discussions it was apparent that we are becoming more dependent on characterization of organisms than on their identification in the classical sense. In this respect, we feel that perhaps the word 'identification' in the regulations would be better replaced by 'identification/characterization.'

With regard to culture collections, we feel they are essential, both for a reference source in the event of some future mishap as well as for a central repository for those not having proper facilities for storage and maintenance of organisms. The two major concerns arising in the discussion of collections were the questions of confidentiality and the cost of establishing and maintaining the collection. Consortia give rise to different problems. Storage procedures usually involve freeze-drying and the risk of losing some members of a consortium because of problems inherent in the maintenance of mixed populations. This problem is compounded when individual members of the consortium have not been identified and you are not able to tell if part of the population has died off or not.

Discussions on risk assessment raised a number of questions. We did recommend that there should be a minimum of data requirements for risk assessment and that these should be set out in the guidelines to the regulations. We questioned whether low probability/high impact events should be considered or even requested of proponents. One might not have the ability to predict such events but perhaps they should be considered as part of the contingency plans and addressed through the ecological effects data. In this respect we would like to ask the group looking at environment data what ecological effects are the important ones to consider in risk assessment evaluation.

We also discussed data bases and their need in the risk assessment process and the apparent problems in existing data banks. We are recommending that Environment Canada work with other departments/agencies, both nationally and internationally, to develop a unique network

in order to coordinate existing data bases or to establish a new data base. As these come on stream and the data availability increases, they will become a major factor in reducing requirements and shortening the risk analysis process.

We feel that the assessment periods that currently exist are adequate in light of similar regulatory requirements on the international scene. We do not think, however, that assessment periods should be immutable. Regulations should be flexible enough to permit reevaluation and readjustment of timing. Regulations should also provide for a parallel public review. We feel that as the public becomes familiar with the process they will become less interested in reviewing all applications and will limit their immediate concern to new and novel applications. The question of confidentiality still exists and some method would have to be found to remove proprietary information.

The data package was also considered and proponents should be encouraged to submit complete packages and not forward data in dribs and drabs as the process moves along. Regulators may deem such information as coming in too late and restart the whole process. We suggest that the guidelines coming out in tandem with the regulations recommend that all proponents meet with EC and H&WC officials to discuss data needs and requirements, and exactly what needs to be submitted.

There are some definitions, or lack of definitions, that trouble us. We have some concern with the inclusion in the microorganism definition of "parts of these microorganisms" and wonder if this might be better moved into a biochemical or byproducts definition. We've also indicated that there is no definition for genetically modified organisms in the regulations. The terms byproducts, toxic intermediates, biochemical products, and secondary metabolites should be defined individually or combined in an all-encompassing definition. We have already referred to the identification of bacteria to the genus level and the possible relevance of the species level. A similar situation exists for algae, fungi, and viruses. At the moment there is a lack of direction on what constitutes a valid identification. Given this, we feel that the guidelines should clarify the identification requirements for microorganisms and indicate the standards of nomenclature to be used.

The term 'field-scale' needs some clarification as to whether the one hectare refers to single sites or the cumulative size of a number of test sites. We feel that if it is cumulative, the test sites would not be big enough to be practical.

We also spent some time discussing markers and pointed out the need for alternate markers to that of antibiotic resistance. High priority should be given to their development.

We also considered who was in the best position to do the identification and characterization of microorganisms. Although the proponent has a vested interest in the product, he is probably in the best position to carry out the characterization and provide the supporting data. Proponents must have the proven ability to undertake such analyses. They must also provide appropriate methodology for identification as well as quality assurance/quality control documentation that allows Environment Canada to confirm and validate the identification and endpoint data. The guidelines should recommend that third-party interpretation be sought by the proponent. We feel that if there is a question on identification, particularly of a new isolate, it would be best to get an external expert involved.

We would like to point out the potential overlap of regulations under different Acts. One scenario we ran through looked at the question of bioremediation using a bacterium that requires the addition of specific nutrients to the environment and possibly the addition of a nitrogen-fixing organism as well. In this case there would be an overlap with the Fertilizers Act of Agriculture Canada which regulates both the mineral nutrients and the *Rhizobium*.

I'm sure this question will come up again and it serves to emphasize the need for Memorandum of Understanding between the various regulatory departments. Thank you.

Rob Quinn, Chairman: -- Thank you David (Major). Are there any questions of clarification?

Seidler: -- In the first part of your presentation, where you were talking about microbial consortia and then the question of identifying genetically engineered organisms to the genus level; would you clarify if you were talking about adding GEM's to a consortia?

Major: -- We don't think there are many people ready to add genetically engineered organisms to a consortium right now because of the problems involved in monitoring. We were really talking about a natural consortium of organisms that could be added to the environment.

Seidler: -- Are you suggesting then that each member of the consortium should be identified to the genus?

Major: -- No, I think it is more important to identify the boundaries of behaviour for the particular consortium. We have to decide what endpoints are useful to define a consortium and then know how the consortium behaves under various conditions in order to predict its behaviour and provide some risk analysis.

Report of SYNDICATE II

HEALTH DATA

Earle Nestmann, Facilitator
Bill Murray, Secretary
Rod Raphael, Secretary

Issues for discussion:

Need for specific endpoints
- **Hypersensitivity**
- **Irritation**
- **Toxicity**
- **Infectivity**

Exposure estimates

Alternate testing strategies
- ***in vivo***
- ***in vitro***

In our discussions we focused on the following four broad issues:

1. A model for CEPA regulations based on the guidelines for microbial pesticides.
2. The need for specific endpoints.
3. The importance of exposure estimates in determining the dose levels of tests.
4. The testing itself.

In testing for health effects we tried to consider what the test substance should be when dealing with consortia, naturally occurring organisms, or genetically modified organisms and so forth, and their characterization.

We spent considerable time discussing regulations versus guidelines. The group as a whole felt that it is extremely important to have a mechanism to modify regulations as the knowledge base expands and our understanding improves. Most of the group, though not all, felt the guidelines for the microbial pesticides serve as a good model. The reason for this is that the pesticide guidelines follow two basic principles. They are flexible for individual products or groups of products and they will continue to develop or mature as the knowledge base grows. Some of the group disagreed with the choice of a model because they felt that the pesticide guidelines were not stringent and forcible enough. Nevertheless, we felt it important to consider how entrenched guidelines or regulations could become.

We discussed the suitability of the proposed endpoints in the regulations, i.e. hypersensitivity, irritation, toxicity, and infectivity. We agreed that these are acceptable but we also recognize that additional testing will be required in some cases. There are certain microbial products, for example, that could produce toxins that have oncogenic potential. Some engineered organisms involving viral sequences are also thought to have this property. Under these circumstances, we felt that the characteristics of these particular microbial products should be examined carefully and should probably call for additional testing. Thus, characteristics

and the background information on the products have to be considered carefully to determine if other endpoints such as chronic toxicity, neurotoxicity, reproductive tests, or behavioural tests are needed. Acceptable testing protocols should be tied to the relevant route of exposure for the human population.

Given all the items that need to be considered in the choice of endpoints and the mixture of results that have to be reported, some consideration should be given to the development of a decision tree. Such a guide is needed to determine what has to be done next when this information becomes part of the package.

We spent a little time discussing the importance of exposure estimates as a means of determining the appropriate level of test material in the health effects tests. One way would be to use the Maximal Exposure Level as the dose. Alternately, we could use the Maximum Tolerated Dose or the Minimal Infectious Dose. We didn't spend a lot of time discussing the pros and cons of these methods but we recognized that there would be cases where one or another would be appropriate or inappropriate.

We didn't go into the question of waivers and when they should or shouldn't apply in any detail. We did feel it was important to emphasize that the data that will satisfy the requirements for the different endpoints has to be information that is available in the literature or data derived directly from the studies. The characteristics of the microbial product itself would help in determining whether or not new or further studies have to be done. Therefore, data may consist of information that already exists or data derived from the study itself plus any information available for clarification purposes.

Our second point is that at the present time regulations specify that *in vivo* tests (animal) should be carried out. We feel that when methodology has developed sufficiently and where it is appropriate to use, alternate *in vitro* tests should be considered by the applicants and regulators.

We had considerable discussion on the capability to monitor organisms after field release. We feel we should have effective methodology for post-release monitoring of these products. This quantification of exposure to humans is important in the event of human health effects in the future.

There was some discussion on how one would treat the organism itself as opposed to a formulated product, a situation analogous to the active ingredient vs. the formulated product in pesticides. We feel it is important that information on the other components of a product be considered in the background information provided. If impurities exist, that is one issue, but if there are other kinds of chemicals present, such as surfactants that could affect the activity of the product, these would need to be considered in the health effects assessment.

Coming back to the previous point on *in vitro* testing or alternate tests, we have a separate recommendation that the regulations should contain a policy statement in support of alternate tests where appropriate and valid. Furthermore, the group suggests that funding for research and validation of such tests should be a priority of the government, if not under CEPA, at least under some other program.

Our next recommendation is really an expansion of a recommendation that appears on page 10 of the Background paper[1] that is part of the proposed regulations document. The recommendation is that humans in contact with a biological product during testing or

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[1] Background Information on Notification Regulations for Biotechnology Products Under the *Canadian Environmental Protection Act*, EC and H&WC, September, 1990.

manufacture should have a medical examination prior to exposure. We feel there should be medical testing both prior to and following exposure to see if there are any detectable human effects. The group did not feel that this recommendation was strong enough as written and suggested that there should be a mandatory medical assessment. This assessment should be done in conjunction with the Joint Occupational Safety and Health (JOSH) Committee and the Biosafety Committee of the group developing the product.

Our final point under testing dealt with cell culture methods which specify cell culture methodology should be used for virus only. We would like to make the point that these methods can be used for other agents and their use should not be limited to viruses.

Finally, we touched on the issue of naturally occurring vs. genetically engineered, several times during our discussion. We didn't feel a distinction between the two is important in determining health effects. When we were asked this morning to consider the testing regimes for consortia we felt the same way; the consortium itself is the test material and it shouldn't be treated differently from other products. We would want to know as much as possible about the biological characteristics, components, and background information on the consortium in order to make appropriate decisions and determine if further tests are required in addition to those specified.

That briefly is a summation of our discussions and the points we have to offer.

Rob Quinn, Chairman: -- Thank you very much Earle. Questions of clarification?

Mes-Hartree: -- I was wondering if your group discussed what exactly should be assessed in a medical assessment or did you just say medical assessment.

Nestmann: -- No, we didn't get into the details.

Report of SYNDICATE III

ENVIRONMENTAL DATA

Ray Seidler, Facilitator
Don Hare, Secretary

The following topics were considered:

1. **Tiering of data and the development of a matrix**
2. **Use/protocols involving microcosms**
3. **Monitoring**
4. **Selection of nontarget substances**
5. **Endpoints/protocols for environmental effects/fate data**

With regard to the need for or the viability of tiering of data, our group came up with the matrix shown below after considerable agony and discussion. I think the main point to emphasize is that tiering seems to be very desirable. Our difficulty was how to break it out, or determine on what principles or bases we were going to use the tiering system. Some wanted to tier on the basis of, if you'll allow this statement, the ecosystem being studied. That is, laboratory tests first, then microcosm, and then the field. We eventually abandoned this for a tier system based on the severity of the dose, a worst case scenario if you will, followed by a range of doses, and then followed by microcosm analyses.

	TOXICOLOGY	FATE	ECOSYSTEM EFFECTS	
Tier I	data base (waiver) high dose non targets		data base (waiver)	
Tier II	dose range plus additional species		microcosm worst case scenario	Industry Efficacy Field Test
Tier III	microcosm		microcosm operational concentration	field release required by regulators

Looking at the matrix, you will see the three tiers along the side, and across the top we have toxicology tests and ecological tests divided into effects and fate. Toxicology we would refer to as single species tests and impacts on beneficial non-target organisms. Remember that the

way the guidelines are presented at the present time, a waiver is theoretically possible at any point in the regulations. Therefore, before toxicology tests are initiated, the proponent or registrant should closely examine the published information and try to negotiate with the regulatory agency on whether tests are, in fact, needed and if so, what kind of toxicology tests are required. You must remember we are not working with pesticidal agents here. We are working with agents involved with bioremediation, waste treatment, mineral leaching, and so on. There is an abundance of literature and published information available. If your agent is a psychrophile for example, why test it in warm-blooded animals?

So if the waiver is not granted, Tier I envisions testing exposure of certain key organisms at high dose levels to evaluate possible toxicology events: - invasiveness, pathogenicity, virulence, death, etc. If there is an indication of need of further testing we would resort to Tier II where the observations would be repeated using a range of doses. In other words, if there is a toxicological response, quantify it and find out at what level the agent is capable of producing the effect, whatever it was, i.e. reproductive, lethal, or whatever. Then, if warranted based on the results of Tier II tests, proceed to evaluation in a microcosm at the so-called field operational concentrations.

On the ecological side, again combining fate, which relates to the persistence, survival, dispersal, genetic exchange propensity, or to ecological effects, we would again like to see a dialogue established between the registrants and the regulatory agencies, again indicating what is available in the literature about the agent under consideration. If it is an aquatic organism and not known to survive in soil, is it really necessary to carry out lengthy terrestrial experiments? However, if the parties cannot agree that a waiver is possible, we would propose a Tier II evaluation in a microcosm setting, again on a worst case basis. A worst case scenario may mean releasing the agent hundreds of thousands times higher than what might be proposed for field tests. I think this is something we envision to vary on a case-by-case basis depending on negotiations between the parties. If undesirable ecological consequences are recorded in Tier II there would be a further test system at Tier III, again in a microcosm at the field release level or field operational concentration of the agent.

Most of the group agreed that the regulators should be offered freedom of flexibility to design the field experiments to answer unresolved questions. Therefore, we might envision that if a field release was to occur there may be specific questions imposed on the test by the regulators. Thus the regulators will reserve the right to have input in the design of certain components of the field trials. In this whole effort then, we wind up with the industry carrying out the tests to evaluate the efficacy of the agent(s) under consideration.

Moving on to the microcosms; if it is deemed necessary, based on the tier system in the matrix outlined, microcosms would be used. They would be deemed necessary when one is unable to address the issues based on laboratory experimental data, when toxicology tests support the use of microcosms, and/or when the general literature is insufficient to grant a waiver. These are the criteria that would trigger the use of a microcosm.

What about the design of the microcosm in terms of its goal? Well, the system should be set up to simulate the environment in a manner that is relevant to the field test. If the field test is in an agricultural setting we would hope that the microcosms would be designed to receive the agent in the same manner that you would release it in the field. If the organism is to be spray-released in the field we would expect it to be spray-released in the microcosm, not coated on the seeds. In other words, be aware or anticipate what would happen in field release.

Design should also reflect relevant concerns. If there is concern in the laboratory tests that genetic exchange with the natural microflora can occur, then be sure to include the natural flora in the microcosm so that the potential genetic exchange can be analysed.

The microcosm should contain species that are relevant to the field test. If the test is for an aquatic system then design an aquatic microcosm. Use a common sense approach.

Environmental control in the microcosm may significantly influence the results obtained. Key parameters that will have overriding influences are temperature and, if soil, the relative humidity and soil moisture. The microcosm should simulate as closely as possible the intended test release site of the agent.

If the eventual release is for an agricultural system, the test may require a disturbed soil system. For example, if the agent is to be released on the surface of disturbed soil, we would suggest that you don't carry out your microcosm experiment using hard-packed soil cores. Sift the soil, repack it into a column, and then say "Aha! the agent is going to infiltrate through the upper layers of soil in the same way it would in the field." In the aquatic situation, you could use continuous flow, once through, or static, whatever most closely parallels the likely release scenario.

On the question of non-target test organism testing; we perceive this as only being necessary after literature review and consultation with the regulators. Again we would stress that these are not pesticidal agents we are looking at, but rather, free-living organisms of the environment that may or may not have been genetically modified.

The selection process for non-target organisms or substances will be based on the following considerations:

1) They should reflect the ecological, economic, and cultural importance of non-target substances and species existing in the intended use target zone or release site.

2) Secondly, we are suggesting that the substance/species should be representative and selected from the following:
    - plants - both aquatic and terrestrial (2)
    - invertebrates - both aquatic and terrestrial (2)
    - fish (2)
    - birds (2)

We are suggesting that two different species from whatever kingdom be included in the test.

We had considerable debate on the availability of the test species. It may be that some key species, present in the area of the proposed release, may be especially sensitive to the commercial product. If these sensitive species are known, they shouldn't be avoided because they are not readily available. It may be necessary to go to the the target site to collect some non-target species that you suspect have a particular sensitivity to the agent.

Moving on to endpoints and protocols for measurement of basic biological, environmental effects, and fate data; ecological experimentation must be carried out in a microcosm. We don't think that ecological tests can be carried out on the laboratory bench in a test tube. We are talking about microcosm experiments and possibly field release sites. Environmental endpoints would include impact of the released agents on respiration kinetics, on the overall health of the ecosystem. How much CO_2 is being respired or fixed? Are there changes in the structure of the ecosystem as determined by population sizes? Are there changes in the composition/diversity of the microbial flora? What is the impact on biomass, whether in a terrestrial or aquatic system? What are the biochemical effects on the system? What changes in key enzymes such as dehydrogenases are present? Does it impact on the physical characteristics of the system? Does it impact on the biogeochemistry of the soil? Does it have an effect on the kinetics of the major soil cycles of carbon, nitrogen, phosphorous,

sulfur, etc.? These are some examples of endpoints that come to mind for ecological effects.

With regard to measuring the fate of the released organism or substance, in particular its persistence, dispersal, and genetic exchange, a concept for an endpoint was presented and discussed. This relates to the need to put some kind of a number or value relevant on the data you may be gathering, its survival, at what level of survival and after how long a period of time. In the case of residual organisms, are a hundred cells too many? Do you need to get down to zero level? Is one thousand enough? Will this level satisfy the regulators? We've tried to back away from hanging our hat on a specific number and are suggesting that fate data for survival may or should be related to the functionally effective level of the organism that was released. For example, if you have released a bacterium that biodegrades a toxic chemical and started out with 10^9 cells per/ml H_20 and it dies away to 10^3 but you know that you need at least 10^7 to be able to measure the biodegradation, we suggest that 10^7 cells may be close to the functionally effective level. If the viable count falls below the functionally effective level, who cares whether the organism is still there? There may be reasons to care, but there may be many reasons not to care. We are suggesting that survival data in relation to fate might be related to the functionally effective level. We think that this concept of a functionally effective level can apply to many if not all parameters of risk assessment. For example, if your agent causes an ecological effect such as lowering the pH of soil at a concentration of 10^8/g soil, but it is only present at a concentration of 10^5, is this still a risk? This functionally effective level provides a principle on which to judge or base your risk assessment.

Another issue for assessing environmental effects is the question of transient vs. prolonged effects. What do we mean by the terms transient and prolonged? As you might expect we had a bit of struggle with the terms. We are suggesting that methods to detect prolonged undesirable changes in the natural ecosystem should relate to a test time frame. Do you mean to carry out this test for a week, a month, a year, or whatever? The time limit should be consistent with the cessation of the product organism's functionally effective level. In other words, you observe an effect, you see it at 10^8 cells/g tissue. How long do you need to monitor to see if that effect is going to persist? How long should you monitor for risk assessment purposes? We are suggesting that you should monitor until the level of the organism drops below the functionally effective level. If the ecosystem is resilient, one would think things would return to normal. However, you would have a real problem if the organism drops below its functionally effective level and you are not seeing a return to normalcy of the ecosystem. This should transmit a clear signal. For example, you could have an agent that biodegrades a toxic chemical and a byproduct of that is lethal for soil fungi. If the agent is effective, the toxic chemical is degraded and the agent dies off to below its effective level. But what about the byproduct of the process that is fungicidal? Does the fungal population return? If it does, you can stop monitoring. Your agent has done its job and the ecosystem has returned to normal. If the fungi do not come back then we suggest there is a significant ecological effect.

This pretty much summarizes our deliberations and I hope I haven't extrapolated too much.

Rob Quinn, Chairman: -- Questions?

Report of SYNDICATE IV

CONTAINED USE

Reg Kucey, Facilitator
and, Secretary

We had a fair bit of fun with our topic. There were some problems with the regulations which many people were quite happy to point out. The focus of our group was on contained use and I'll try to outline our concerns in the order of what we thought was their importance. We looked at the definitions first, recognizing the need for clarification if we were going to do them justice in our discussions.

First, and this has been brought up previously, is the definition of a microorganism, particularly in respect to inclusion of 'parts of these microorganisms' that appears in the interpretation section of the proposed regulations. This is of particular importance to contained use where the level of containment of a very toxic pathogen may be at level four and where you have restricted access to laboratories. However, when the organism is fractionated into various organelles, or enzymes isolated from it, further studies may no longer need the high containment level for work with such fractions. I think you can see the implications of having 'parts of microorganisms' as part of the definition. We also feel there should be consistency with other recognized definitions for microorganisms to avoid confusion. We accept the definition for contained facility and that the levels of containment should be consistent with the Medical Research Council (MRC) guidelines.

We wondered if 'contained production,' in conjunction with the existing definition of microorganism which includes 'parts,' means that the entire process would have to be carried out in a confined facility. If the definition of microorganism is modified, the question could probably be answered. We feel that only the live viable organism would have to be produced and handled at a certain level of containment. When you are no longer dealing with viable material you should no longer require the same level.

Under the definition for 'contained use' we wondered if greenhouses, barns, and such-like which can be considered as semi-contained at best, qualify as contained facilities or are they considered as part of field introduction? We had arguments for and against and as it actually turned out, we found, in two different places in the proposed regulations, one case considered as a field introduction and in the other as a contained facility. This should be clarified. We were also concerned as to whether GILSP were adequate procedures for contained use.

The second main point we felt required our attention was that of the 'quantity trigger for exemption.' At the present time R&D is exempt from notification if one is working with quantities of 10 litres or less. Ten litres is the volume that was proposed in 1976 according to our information, and it was an amount that was accepted but not agreed to. We feel that 10 L is too small a volume for routine development. In 1976 the level of technology was much less than it is today and, as a number of people in the group mentioned, they are routinely carrying out 250 L fermentations. We feel there should be exemptions for 80-90% of the contained productions going on. It is only the very large scale or unusual procedures that should require notification. This would greatly reduce the notifications required for R&D.

We felt that the trigger level should be tiered depending on the risk involved. A yeast may well be cultured routinely at levels of 250-500 L with no problems at all because of the low risk. On the other hand, as someone has already mentioned, a 10 L culture of *Bacillus*

anthracis poses considerable risk. It is not a question of whether 10 L is acceptable and 11 L is not. Levels should be consistent with risk assessment and again we are suggesting the Laboratory Biosafety Guidelines for risk assessment.

We also felt there should be some clarification with respect to methods such as continuous culture. If we have a 10 L fermenter turning out 50 L a day, is it considered a 10 L system? In the same vein, are 10 - 10 L flasks on the bench considered a 100 L system? This isn't really spelled out.

It was pointed out to us that the level itself is the only requirement necessary for an exemption in CEPA. We are not able to say there is an unlimited fermentation level for R&D but a level has to be presented. In this respect, we feel a quantity exemption should be based on a tiered system of risk assessment.

We had considerable discussion on Biosafety Committees and, as I have indicated on the overhead, I will refer to this as the Biosafety Committee/Risk Assessment Mechanism (BC/RAM). The reason is that some of the group had difficulty with the connotation of biosafety, and felt more comfortable thinking there was a mechanism for the evaluation of risk.

With respect to these committees, the first question we asked was whether it was legally possible to have a Biosafety Committee when there is no mention of it in the Act. We feel that EC should ask themselves whether they can legally require such a committee. We agreed that it is not necessary to legislate it and assumed that the option of having a Biosafety Committee/Risk Assessment Mechanism and its associated implications would be adequate. At the present time you have to have a Biosafety Committee and adhere to the biosafety guidelines to qualify for an exemption. It goes without saying then, that in order to do a biosafety risk assessment you have to have some risk assessment mechanism in place.

We also wondered if Environment Canada can legally set out the duties of a Biosafety Committee/Risk Assessment Mechanism or is the committee strictly an advisory body? In the event of a mishap, would the Biosafety Committee be considered legally responsible for what happened? We do not feel that this authority can be delegated to a Biosafety Committee. In this event, they would be an advisory body and need terms of reference outlining the minimum qualifications of a BC/RAM. These guidelines should give sufficient flexibility so that each organization would be able to tailor the Biosafety Committee or Risk Assessment Mechanism to their own particular requirements. The role and reports that the Biosafety Committee would be involved in would have to be consistent with these terms of reference spelled out in the guidelines, i.e. they would look at contingency plans, they would look at procedural matters, etc. These things would all be spelled out in the guidelines.

We would also like to point out the potential conflict of interest with a Risk Assessment Mechanism that is part of the company. You could have a scenario where a researcher on the company's Biosafety Committee may have to shut down his own lab because it has been judged unsafe. Although the Occupational Health and Safety guidelines would provide some protection, there is still potential for conflict.

Confidentiality must be protected and respected as well. If annual reports of the Biosafety Committee were required by Environment Canada these should be confidential and not available through Access of Information processes, etc.

The Risk Assessment Mechanism should be inherent in an organization and not imposed by Environment Canada. We are not saying that Environment Canada should have a huge cadre of inspectors to carry out the risk assessments for everyone. The mechanisms should be on-going within the organizations.

The Risk Assessment Mechanisms should be flexible and there should be a clarification of the roles and responsibilities of the Biosafety Committee/Risk Assessment Mechanism and the Joint Occupational Safety and Health Committee.

For risk assessment itself we feel there is a definite need for protocols and guidelines. Whether the existing ones are sufficient or whether further development is needed we have to have appropriate guidelines that require the minimum of interpretation by individuals. Guidelines should be applicable on a case-by-case basis and not provide blanket coverage for all eventualities. We recognize that for every organism fermented or genetically modified there will be different requirements for risk analysis.

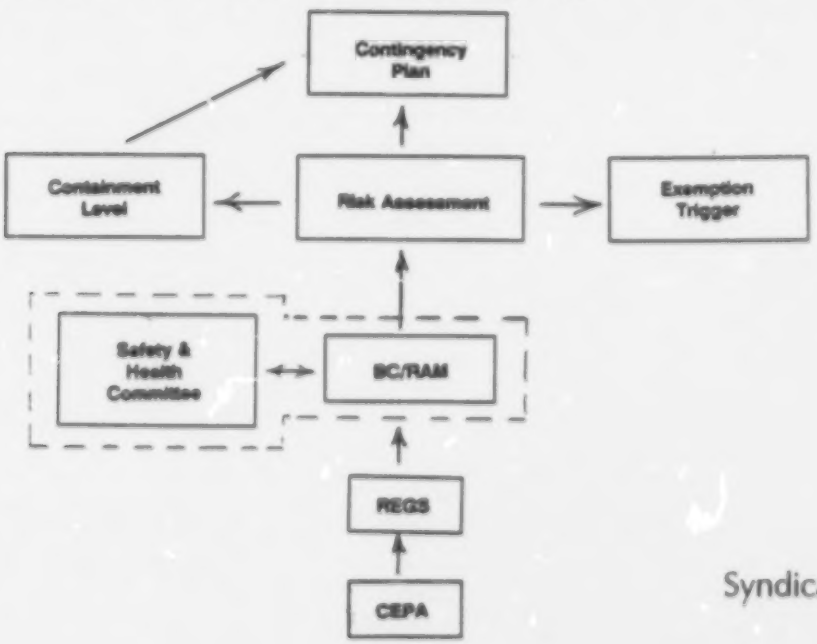
The risk assessment should influence the containment level necessary, the quantity trigger for exemption, and the extent of the contingency plan in the event of a mishap. The risk assessment should be conducted by the Biosafety Committee or other Risk Assessment Mechanism, and the Environment Canada inspector's role should only be for verification.

It was pointed out that there was a potential for overlap of duties of the Biosafety Committee/Risk Assessment Mechanism and the JOSH Committee. Duties should be clearly defined for both.

We all agreed that contingency plans were a necessary part of the process and should be dependent on the risk assessment.

We have a couple of minor suggestions. It is felt that in the next draft of the regulations it would help if pages were numbered consecutively so that we could tell the difference between page 2 of the Notification Regulations and page 2 of Schedule XI and page 2 of Schedule XVI, etc. A question and answer booklet should be considered for some of the common questions arising.

The diagram roughly illustrates how we felt it all went together. The regulations would be derived from CEPA and these regulations would allow us to do a risk assessment within an organization. This risk assessment mechanism should have clarification of its roles and responsibilities both for the Biosafety Committee/Risk Assessment Mechanism and the Safety and Health Committee. The two committees could be combined, we had no difficulty with this. Risk assessment can affect the exemption trigger and the containment level, both risk assessment and containment level can affect the contingency plan.



Report of SYNDICATE V

SCOPE OF REGULATIONS

Wendy Sexsmith, Facilitator
Mary Mes-Hartree, Facilitator
Mark D. Bishop, Secretary

We had a fairly large group and, as has been pointed out, we raised quite a number of issues. We finally boiled these down to four main topics: the objectives of CEPA, assessment procedures, the Domestic Substances List and Schedule XVI, and public information.

We spent quite a bit of time discussing CEPA, what is being covered under the Act, and how it is being regulated. This gave rise to a number of questions and consequent recommendations.

A major concern was the failure to delineate the other Acts that regulate biotechnology products and we feel that these should be spelled out in the preamble of the regulatory guidelines for CEPA.

At the same time, there should be clarification with respect to products, timing, state of development, and range of use.

There was concern with the overlap of other Acts which also regulate biotechnology products and the different regulatory requirements developed for these Acts. We strongly recommend harmonization of data requirements at the federal level, with one window to government so that industry would know where to go.

At the same time, to avoid duplication of regulations we would encourage federal/ provincial cooperation on all issues.

Another point that was raised under the discussion of the Act was contained use and what it really meant. Our recommendations concerning contained use are: 1) to define and clarify the 10 L quantity specified and, 2) to provide guidelines for the structure and mandates of Biosafety Committees.

You will note that we had a lot of 'to clarifies' which must tell the regulators something. We'd like clarification on what organisms are regulated under CEPA. There appears to be a lot of confusion with respect to plants, animals, and multicellular organisms. There is something in the back of the regulation document that deals with this but the meaning is not clear. We also wonder why medical and veterinary diagnostics are excluded under the regulations. We need clarification on what is to be done with products presently in the field or in the advanced research stage.

Under assessment procedures we had two generalized areas to discuss. First, the questions of genetically modified organisms and naturally occurring organisms and second, the whole issue of risk and the tiering system. We spent a lot of time discussing whether we needed to consider genetically engineered organisms and naturally occurring organisms separately under the CEPA regulations. While no consensus was reached, it did become apparent that what we were really discussing was risk and the risk assessment procedure.

The general feeling of the group was that with the regulations as they stand now, the tier approach is based on the scale of production and whether you are dealing with 10 L or at commercial scale. We feel the element of risk is as important as volume or the production stage.

With respect to the type of organisms, we feel that the issue is not so much whether the organism is genetically modified or not, but what the risk is in using that organism. These are two of the underlying thoughts of the group on the issue of assessment.

We are recommending that the CEPA requirements identify exactly what procedures they propose to use in risk identification and risk assessment and ensure that these procedures are reviewed and receive consensus from the stake holders. Furthermore, the risk assessment procedure should be linked to the stage of development. This area has also been touched on by some of the other syndicates.

We would also like to be apprised of the criteria for exclusion of an organism. At the moment it would appear that CEPA intends to catch all organisms and then exclude. What are the rules for differentiating between risky and innocuous organisms? Knowing how this is done would save us from doing a lot of research on organisms with limited risk.

The next issue we discussed was the waiver system. As it stands, you would have to publish in the Gazette to obtain a waiver, and industry has difficulty with confidentiality using this procedure. Linked to this is the public perception that industry is trying to get out of doing research by obtaining a waiver. More will be said about waivers when the Domestic Substances List (DSL) and Schedule XVI are discussed. As it stands now the waiver system is virtually unusable.

Time frames for review were also discussed and, unlike one of the other syndicates, we feel that the time periods are too long. This is particularly true for applications using technology that gives rise to fast turnovers. Bioremediation technology for example, where you may go out into the field and pick up an organism, grow it in the lab and be ready to go back out again in three months. Here, a 270 day assessment period would not be acceptable.

Our recommendation for time periods is that Environment Canada should acknowledge:

- when the submission is received
- when the data package is complete so that you know when the time clock is starting
- when the review is complete. If you had a fairly innocuous organism you should not have to wait the full 270 days if Environment Canada can see immediately that it is not going to pose a problem

This latter point again comes back to the whole issue of risk, and can we eliminate further testing of those organisms that don't pose risk. What we are looking for is some mechanism for excluding 'safe products' so that we don't have all new biotechnology products going through whole testing procedures.

The final major issue in this section had to deal with competitiveness and the need for international harmonization in the regulatory processes. We must maintain a favourable position for Canadian developments in biotechnology in relation to outside competition, not only from the standpoint of biotechnology products *per se*, but also in relation to non-biotech products which may be competing for the same niche. This again relates back to those people using organisms for bioremediation who have to compete with other remediation technology.

It was apparent in our discussions on the DSL and Schedule XVI that there is general dissatisfaction. In this respect, we are recommending that a working group be set up immediately to find some way to make the DSL and Schedule XVI listing procedures workable. This working group should be comprised of industry, government, research, and the public. One of the big problems with these lists is that of identification and maybe CEPA should look into the use of general categories as in EPA's Toxic Substances and Control Act. One suggestion for dealing with the problem is to consider identification by strain designation and deposit number in a recognized culture collection.

The final issue we discussed dealt with public information. There were two general areas of discussion. One was how does the public get information on what has or has not gone through the notification procedure. The recommendation was made that there should be a list developed of products that have gone through the notification process and that are available commercially. It was also recommended that a code number should be assigned to each product as it comes into EC and this number be used to identify it during all stages of development and use. This code would allow consumers to know that the product had gone through the notification procedure and it would also provide a code system for the field testing.

We are also recommending a notification process for the provinces, provincial jurisdictions, and the public, of up-and-coming field research. We feel it is important to get the public involved at the earliest possible stage of the process so that we don't end up with a lot of public backlash after having gone through it. We have to be proactive, we have to have the public involved early in the regulation process. The public has to see that its advice is actively sought and respected by regulators and advisory committees developing regulations and guidelines.

I think these points summarize our discussions over the past two days.

GENERAL DISCUSSION OF SYNDICATE PRESENTATIONS

Rob Quinn, Chairman: -- Ladies and gentlemen...it is now 3:30 and we would like to finish by 4:30 knowing that some of you have planes to catch. The agenda calls for a continuation of the reports and a round-up discussion which gives us some flexibility. We've finished the reports and we've had some clarification questions so I think I can now open the floor to general questions. I would ask you to put your questions as briefly as possible, with a minimum of preamble. Please direct your question to a specific panelist or to me for redirection. You are at liberty to state your agreement or disagreement with particular points, to ask for further clarification of some of the points discussed, or to query where we go from here. I think this is about as much as we can do at the moment. So, if there are questions please step up to the microphones. Do we have an opening question?

Rushforth: -- Although I am not in favour of the ecozone concept of registration, I noticed that there was no discussion on this. Could someone comment on that?

Sexsmith: -- For starters, in our group we didn't really discuss the ecozone concept or indigenous vs. imported in any specific way, although it was raised under the assessment procedures. There was discussion revolving around the concern about the assessment procedures and leading into whether or not there should be some mechanism to screen natural vs. genetically altered, and indigenous vs. imported, and that sort of thing. We ended up, as you've heard, in not dealing with it specifically.

Seidler: -- It came up briefly in the environmental group and was avoided like the plague, and I think it should be.

Quinn: -- I would like to ask a question of someone on the panel or of members of Environment Canada or Health and Welfare Canada who have been directly involved with these regulations. As I listened to the presentations I kept writing down little notes and when I refer back to them I find that the word "risk" has been mentioned in practically all of the presentations. The question I think that might be suitably asked is, should this be the basis of the next draft of the regulations; tiering by risk, concentrating on that which needs concentration and screening out that which doesn't?

Kucey: -- I think in our committee it was very definite that we thought risk was the prime concern with respect to a number of issues: to the containment level necessary for the work with that organism, as the trigger for whether or not you had to notify Environment Canada, or whether you got an exemption. We did not think that it was really consistent with any science to have this same criteria put on to a human pathogen as opposed, say, to something that is going to fix nitrogen with legumes. We definitely put risk as a very high priority.

Mes-Hartree: -- In a lot of the issues we discussed, especially when we were going through the genetic modification, natural, indigenous or imported, it all came down to risk. We found that risk was an underlying issue in a lot of the things that we brought forth when it came to review; when it came to exclusions/exemptions. A lot of the syndicates have said the same thing and I suppose your question is really directed to Environment Canada to determine what they will do from here on.

Quinn: -- I don't mean to put people on the spot because I don't think they can give a firm

reply but perhaps it wouldn't hurt to have some exposure to their thinking on the subject. Is there a volunteer from Environment Canada?

McIntyre: -- I think, as the Chairman correctly pointed out, the question of risk is of major concern, not only in Environment Canada but with Health and Welfare Canada as well. I want to reiterate that the whole intention of our presence here the last two days is to listen to your concerns and get a better appreciation of what you feel to be some of the outstanding difficulties associated with the regulations. Give us sufficient grist, and I think you have given us a supply, and we'll go back to the mill to see where we go from here. Needless to say, any and all of the comments raised during the sessions here will be considered.

Quinn: -- Perhaps on behalf of the audience I might ask if you can give some target date when you might provide us with some reaction or response to the points raised? I don't mean a new draft, but simply an indication of what you think you are going to do in respect to the issues raised.

McIntyre: -- My immediate reaction is that you've given us an awful lot to think about. I don't think that at this point in time I can refer to any other date than that John Buccini referred to in his presentation. In the Green Plan it has been identified that the regulatory regime for biotechnology will be in place by 1992.

Quinn: -- Well the Green Plan has had one revision already, so that might be a tall order. I guess what I was getting at and what I sensed from the discussions over coffee the past couple of days, is that there has been a lot of hard work put into this by yourselves and those present. I think what they're looking for is a target date that you might shoot for initially to give us an idea of what points you've adopted which are different from your own, not necessarily the draft regulation on how you reflect that point, but where there might be changes so that the whole thing doesn't come back again umpteen months from now in a new draft without our knowing your changes of thinking in the meantime.

McIntyre: -- As I indicated earlier, it was my first exposure to a lot of the information that we've received in the plenary sessions. I was privy to the information in the syndicates where I participated but not to all of what has just been presented. Obviously we are going to require dialogue and consultation with our counterparts at Health and Welfare Canada who have also just been faced with the issues raised. Given this, I don't think we can lock ourselves into a date as to when the next draft of the regulations will come out, other than I think it is safe to say that the next draft will reflect some of what has been raised over the past two days.

Quinn: -- I wasn't so much looking at a date for the next draft but rather the timing for a response to what you have learned here. Let me pose another question. How does the notion strike you of the proposed working group involving industry, government, the public and so forth, to start looking at the DSL?

McIntyre: -- As I've indicated, we're open to any recommendations or suggestions that have been made. Perhaps Dr. John Smith of Health and Welfare Canada should be given the opportunity to respond to these questions as well.

Quinn: -- Certainly.

McIntyre: -- I should indicate too, when you asked me earlier if I could give a succinct answer as to what I have learned here. I've learned a lot in the past couple of days of this very fruitful exercise.

John Smith: -- As Terry (McIntyre) has said, we are here to listen to your recommendations

and we are now in a position to take these back and use them in conjunction with things we have been thinking about. My understanding is that the plan is for us to identify those areas in which some consensus has been reached which meet our needs, and on that basis redraft the regulations. We will also identify those areas which are still under contention. Then we will determine the proper mechanisms to make revisions and to continue the consultation process. As John Buccini mentioned yesterday, there will be room for further consultation. In the interest of fairness to the complex issues that these regulations deal with, it would probably be inappropriate for either of us to come back and let you know what our position is on something that we have just heard this afternoon.

Quinn: -- Questions?

Wearing: -- A question for Ray Seidler. You mentioned that your syndicate spent about 80 percent of its time on the question of tiering by risk. I suspect you spent more time back with the Environmental Protection Agency in that area. My question is, did you at any time consider ignoring tiering and putting all products on an equal basis?

Seidler: -- Could I have you repeat one part of that.....tiering by risk as opposed to?

Wearing: -- ...all having equal data requirements.

Seidler: -- All what?

Wearing: -- All products. In other words, have no risk gradation or risk tiering.

Seidler: -- Actually I've spent very little time, certainly no time in the past four years, putting any suggestions into the regulatory process in EPA. I'm a researcher in the Office of Research and Development. What you've heard should reflect my personal experiences and prejudices and I hope this can be said for the whole group during the evolution of the matrix. I'm trying to speak on behalf of the group without really knowing their attitude on this. My perception is that it is not fair to use the term 'tiering by risk.' I was never consciously aware that that indeed was what we were doing. The evolution of the matrix was a struggle. Some of us, myself included, wanted to tier on the basis of the ecosystem in which the tests were being conducted, i.e. in the laboratory vs. the microcosm vs. the field. There were several components of this that we had difficulty in finding a home for. Others suggested that we reconsider tiering in a direction that evolved today, i.e. with a tier I, II, and III on one axis and the other axis related to toxicology and ecological testing. I think that the evolution of the tier we obtained integrates components of natural subdivisions. The ecology side vs. the toxicology side and then it integrates or imposes or superimposes on that breakdown the worst-case scenario. I don't really relate that to risk although I can see how someone else might. I don't consciously relate conducting the first round preliminaries of worst-case scenarios as related to level of risk. I haven't really thought about it in that way. I think the consensus in our group would be that this seems to be a logical, effective approach in demonstrating the properties of a particular commercial product. The least expenditure of time, effort, and resources, or the biggest bang for the buck. I hope this summarizes the group's feelings. Certainly, no one in the group consciously used the term 'tiering' based on risk. I never really thought about that until you brought it up.

Wearing: -- That is exactly the point I hoped you would come to because I see this as being optimum for both government and industry. Time, resources, and cost-effectiveness.

Quinn: -- Another question?

Bishop: -- In the group that I was in there were people present from Ontario and they indicated that in the province they had not established any regulations at this point in time.

I'm now curious. I saw representatives here from the Province of Quebec, and there might be other provinces represented. I'm wondering if they have established any regulations of this nature.

Sexsmith: -- I'm from New Brunswick. We have no specific regulations at present for biotechnology although we have pieces of legislation that act as catchalls. The bioremediation comes through us through the Environmental Impact Assessment (EIA), or through the Clean Environment Act, or can be picked up under the Clean Water Act. However, there is no specific legislation at this time.

Stuart Bailey: -- Just to clarify for the record: although we do not have legislation which specifically addresses biotechnology at this time, we do have other legislation that impinges upon biotechnology, or legislation that can apply indirectly. One of the things we are doing in Ontario is assessing the need for provincial biotechnology legislation and a lot of this depends on what is happening at the federal level.

Gaucher: -- I'm representing Environment Quebec. We are in about the same position as Ontario at the present time. Part of the Pesticide Act in Quebec will cover biopesticides. There are also general provisions in the Environmental Quality Act which can be used to control field trials and have some certification process there. However, we are starting to think about specific legislation for biotechnology and its products.

Quinn: -- Any more questions? I suspect you've all worked hard the past couple of days and we might close off at this point. But before we do, I think we might show our appreciation for Terry McIntyre and John Smith, and particularly Sheila Forsyth, for all the hard work that has been put into this conference.

With that, unless there is something further anyone wishes to say, we'll close and look forward to your response to our deliberations and the Proceedings. Thank you very much.

RECOMMENDATIONS

Issue	Recommendations	Concerns/Comments
Canadian Environmental Protection Act		
Scope of Regulations and Guidelines	- clarification of what CEPA covers in the preamble to regulatory guidelines.	- products not covered under existing legislation. Residual authority if other Acts do not regulate.
	- listing of other Acts regulating products of biotechnology.	- agricultural products, eg. transgenic plants, biological herbicides, insecticides, fungicides, plant growth promoting organisms, veterinary vaccines, biologics. Human health products, Food and Drugs Act.
	- harmonization of data requirements with other regulatory processes (PCPA, etc.).	- flexibility better maintained in guidelines.
	- a mechanism to modify regulations /guidelines if needed.	- to accommodate expanding knowledge base. Pesticide guidelines suggested as model though possibly not stringent or sufficiently forcible.
	- retain flexibility of regulations.	
	- one window to government for industry.	- one department to coordinate all reviews - the "front office."
	- federal/provincial cooperation at early stage.	
	- inclusion of identification and nomenclature requirements for microorganisms.	
Microorganisms		
Definitions	- clarification of microorganism interpretation with particular reference to "parts thereof."	- implications of same level of containment for viable organisms and their isolated components, i.e. organelles, enzymes. Special needs for genetic elements?
	- clarification of byproducts, toxic intermediates, secondary metabolites etc.	

Issue	Recommendations	Concerns/Comments
Microorganisms *cont.*		
Identification/Characterization	*Pure cultures* - genus level at least. - more precise ID with increased risk.	- known pathogens. - genetic elements should also be characterized since they are considered in risk assessment and monitoring.
	ID endpoints - closeness to known taxonomic groups. - functional tests.	
	Methods of ID - classical cultural, biochemical - PLFA - rRNA - DNA - MAb - phage	- more dependence on the characterization of an organism than on identification in the classical sense. - requirement for position on alternate markers to antibiotic resistance.
	Consortia - describe characteristics of consortium as a whole - not component spp.	- patenting could require more precise information on consortium components and attributes.
	- more precise ID of spp. if pathogens present.	- more R&D needed on application of new ID technologies to mixed populations of the consortium.
	- minimum of human/animal health data. - identification/characterization as per pure cultures.	
Identifiers	- proponents with proven ability with a requirement for third party interpretation.	- must produce methodology for ID and QA/QC documentation to allow EC to verify ID and endpoint data.
Culture Collections	- establishment as reference repository.	- question of confidentiality. - cost of central culture collection facility. - vulnerability of mixed populations to change in respect to maintenance of consortia.

Issue	Recommendations	Concerns/Comments
Contained Use		
Contained facilities	- as per Laboratory Safety Guidelines, 1990.	
Contained production	- clarification of total production contained or only contained during "viable" stage.	- level of containment required should decrease when organism no longer viable.
Contained use	- clarification of greenhouses, barns, etc. Field introduction or contained facility?	- is GILSP adequate for contained use?
Quantity trigger for exemption	- trigger level tiered based on risk assessment. - only very large scale or unusual procedures require notification. - clarification of continuous flow processes and multiple batch procedures. - levels must be presented.	- levels consistent with risk. - 10 L volume exemption outdated.
Risk		
Evaluation of risk	- a tiered evaluation system based on a case-by-case analysis to include: - potential risks of proposed use - scale of use - availability of extant data. - resources required for identification.	- risk assessment will influence containment level, quantity trigger, and extent of contingency plans.
Assessment of risk	- minimum of data requirements for risk.	- set out in guidelines to regulations.
	- Environment Canada to specify procedures for risk identification/assessment.	- concurrence of stake holders required.
	- risk assessment to be undertaken by Biosafety Committee or other mechanism.	- EC inspection for verification only.
	- Environment Canada to develop a data base that can be used to establish risk.	- develop in conjunction with national and international agencies. To expedite risk analysis process.
	- contingency plans as part of process.	- address low probability/high impact events through contingency plans.

Issue	Recommendations	Concerns/Comments
Risk		
Assessment *cont.*	- assessment linked to stage of development.	
	- use of risk over volume at production stage.	- present approach no longer viable.
	- focus on organism posing risk.	- GEM or NOM not the issue but what is of concern. How to differentiate between innocuous and risky?
	- clarification of what is to be done with products already in the field or in advanced stages of research.	
Data Packages	- that registrants and EC/HWC meet prior to submission.	- encourage registrants to submit complete data packages.
	- acknowledgement by Environment Canada when: - submission is received. - data package is complete (start clock). - review is complete.	
Assessment Periods - Time Frames	- need mechanism for safe product exclusion.	- present 270 days too long for innocuous product.
	- flexibility for readjustment of periods.	- expectation of shorter periods with increased knowledge base.
Waivers/Exclusions	- clarification of requirements for exclusion of organisms.	
	- no distinction between genetically modified and naturally occurring organisms.	- focus on organisms posing risk. Differentiate between innocuous and risky.
	- registrants to carefully examine all available data prior to advanced testing to establish possibility of waiver.	- waivers pose difficulties for industry in confidentiality and public perception.

Issue	Recommendations	Concerns/Comments
Domestic Substances List (DSL) and Schedule XVI	- Environment Canada to immediately establish a working group comprised of industry, government, academia, etc. representatives to establish DSL and Schedule XVI lists with respect to biotechnology products.	- problems with identification. Suggest looking at general categories (EPA-TSCA). - consider identification by strain designation and deposit number in recognized repository.
Biosafety Committees (Risk Assessment Mechanism)	- clarification of legality.	- doesn't appear in the Act.
	- an advisory body only.	- not subject to legal action for mishaps.
	- terms of reference with minimum qualifications of Biosafety Committee or "Risk Assessment Mechanism" to come from Environment Canada.	- responsible for procedural matters, contingency plans, annual reports etc. as spelled out. - confidentiality of reports a concern.
	- guidelines to be clear and require the minimum of interpretation.	
	- guidelines to be on case-by-case basis and not given to blanket coverage.	- conflict of interest a potential problem for members of organization's Biosafety Committee.
	- guidelines to be flexible to permit organization to tailor committee to their particular requirements.	- inherent part of organization and not imposed by Environment Canada.
	- organizations clarify responsibilities of Joint Occupational Safety and Health Committee and the Biosafety Committee.	
Health Data Endpoints	- hypersensitivity, irritability, toxicity and infectivity acceptable but other endpoints may be required.	- other endpoints such as chronic toxicity, neurotoxicity, behaviourial tests, may be required for certain products.
	- testing to be tied to route of exposure. - development of decision trees.	- guidelines to the next step.

Issue	Recommendations	Concerns/Comments
Health Data *cont.*		
Exposure estimates	- use of Maximum Exposure Level, Maximum Tolerated Dose, and Minimal Infectious Level, as guidelines - one or another as appropriate.	
Data requirements	- data to satisfy required endpoints to come from literature, research data, and other clarification information.	
In vivo testing	- regulations should recognize that new *in vitro* tests could replace animal testing in some instances.	
Alternate tests	- regulations should support alternate testing where valid.	- research on validation tests should be a priority of government.
Cell culture methodology	- methodology not be limited to viruses.	- techniques are useful for other organisms as well.
Human exposure	- mandatory medical assessment prior to, and following exposure. - effective methodology be developed for post release monitoring of human exposure.	- assessment to be done in conjunction with Biosafety/JOSH Committees.
Organisms vs. formulated product	- requirement for information on all components of formulated products.	- important if components influence activity, persistence, etc. of active ingredient.
Consortia	- consortium to be considered as single entity as for any product.	- as for any organism a full data package is required for decisions on further testing, etc.
Environmental Data		
Tiering of data	- tiered testing to progressively evaluate quantitative ecological and toxicological effects.	- establish ecological or toxicological effects at high dose (worst case) of key organism followed by a second level using a range of doses to quantitate response. - for ecological testing proceed to microcosm to evaluate field response concentrations.

Issue	Recommendations	Concerns/Comments
Microcosms		
Use of	- use when unable to address the issues on the basis of laboratory data, when toxicological data support their use, and when literature is not complete.	
Design of	- should simulate environment relative to field test.	- terrestrial, aquatic, relevant species, method of release, etc.
	- should accommodate special concerns - genetic exchange with indigenous flora.	- ensure that natural flora is present in the microcosm.
	- should use sensitive species of proposed release site even though not readily available.	- may be necessary to collect from target site.
Non-target test organisms	- should reflect ecological, economic, and cultural importance of non-targets in intended use zone.	
	- two species to be selected from representative plants, animals, fish, birds.	
Field Trials		
Design	- regulators reserve right to design components of field trials.	- necessary to answer any unresolved questions. - industry to carry out tests to evaluate efficacy of agents under consideration.
	- small-scale trial size of 1 hectare - too small if cumulative.	- single site or sum of a number of sites?
Environmental Effects and Fate		
Endpoints	- use of endpoints reflecting impact of agent on the health of the ecosystem.	- environmental endpoints reflected in respiration, population size, population composition, biomass, enzyme changes, physical characteristics, major element cycles
		- environmental fate reflects survival at functionally effective level, transient vs. prolonged, background levels.

Issue	Recommendations	Concerns/Comments
Environmental Effects and Fate *cont.*		
Evaluation	- need to establish functionally effective levels.	- a level below which the product (organism) no longer presents a risk.
	- fate data for survival should be related to functionally effective levels.	- functionally effective levels can apply to most if not all parameters of risk assessment.
	- detection of prolonged undesirable changes should relate to test time frame and be consistent with the organism falling below the functionally effective level.	- monitor until level drops below functionally effective level. - transient effects reflected in ecosystem returning to normal.
The Public Interface	- establishment of a review process with public input.	- confidentiality a concern.
	- development of a list of products that have gone through the notification process and are available commercially.	- concern that the public is not getting information and is not aware of what is going on.
	- Environment Canada to assign a code number to each product that is submitted.	- code will allow consumers to know product has gone through the notification process and will provide a ready ID in field testing.
	- a notification process for provinces, provincial jurisdictions, and public, of upcoming field research.	- need to be proactive and involve public early in the process.
Commercial Competition	- international harmonization to provide favourable footing for Canadian biotechnology products.	- competitiveness with trading partners both in relation to other biotechnology products and non-biotech products competing for the same niche.

APPENDICES

BACKGROUND INFORMATION ON NOTIFICATION REGULATIONS FOR BIOTECHNOLOGY PRODUCTS UNDER THE *CANADIAN ENVIRONMENTAL PROTECTION ACT*

SEPTEMBER 1990

ENVIRONMENT CANADA

HEALTH AND WELFARE CANADA

INTRODUCTION

Biotechnology and the *Canadian Environmental Protection Act*

The *Canadian Environmental Protection Act* (CEPA), passed into law on June 30, 1988, contains provisions for the assessment of environmental and health effects of substances new to Canada prior to manufacture or importation. In this way, substances entering the environment or being introduced into Canadian commerce which could pose potential hazards to the environment or human health will be identified and controlled from the outset.

The basis for the assessment of new substances was the Final Report of the Environmental Contaminants Act Amendments Consultative Committee (Minister of Environment and Minister of National Health and Welfare, 1986), which contained recommendations to increase the federal government's ability to deal with environmental contaminants. This report outlined a system for notification and first assessment of new chemicals entering Canadian commerce. The report also recommended that the *Environmental Contaminants Act* in its amended version cover biotechnology,(see appendix A for definition of biotechnology in CEPA) microorganisms and related issues not formally addressed by the Committee. The broad definition of "substance" (see appendix A for definition of "substance" in CEPA) eventually provided in CEPA reflects this recommendation.

In December 1987, as a part of the consultation process associated with the development of the *Canadian Environmental Protection Act* (CEPA), a discussion paper setting out proposals for regulating biotechnology was released for public comment and discussion. This process culminated in a workshop in November 1988, which reviewed and addressed the areas of concern raised during the consultative process. These areas of concern have been addressed by Environment Canada and Health and Welfare Canada through the drafting of regulations which more closely reflect the process by which a biotechnology product is brought to commercialization. The diversity of applications and of organisms requiring assessment under CEPA will require flexibility in the assessment process. This flexibility has been incorporated in the regulations.

CEPA defines a new substance as one not on the Domestic Substances list (DSL). The DSL to be published in the Canada Gazette at the end of this year will not contain any biotechnology products. Consequently, all biotechnology products will be considered "new substances" and notifiable under the proposed new substances notification regulations. However, should manufacturers or importers provide satisfactory evidence to substantiate that specific products were in commerce in Canada between January 1, 1984 and December 31, 1986, consideration will be given to including these on the DSL. In addition, certain biotechnology products may have an established safety record when used for

specific purposes. Schedule XVI of the draft regulations has been incorporated to provide the mechanisms to exempt such products from notification.

Notification under CEPA is not required for a substance regulated under any other Act of Parliament that provides for (i) notice to be given prior to manufacture, import or sale, and (ii) an assessment of whether it is toxic (see appendix A for definition of "toxic" in CEPA).

A proponent's responsibilities are fulfilled once the prescribed information has been submitted and assessed. However, if during the assessment, health or environmental hazards are identified, a number of further actions are possible including requests for additional information or controls on the use of the substance.

GENERAL PROVISIONS

- Products assessed under the proposed Regulations include microorganisms to be used in a variety of applications such as, but not limited to, bioremediation, mineral leaching, degradation of chemicals, cloud seeding, waste treatment, waste disposal, chemical production, lignin degradation, microbial enhanced oil recovery, biosensors, and energy production.

- An iterative and staged approach to notification and provision of information is used, based on the stages of development of the product. Corresponding information requirements and assessment periods build on those of the previous stage of notification.

- Notification is required prior to manufacture or importation for contained uses beyond the scale of laboratory research.

- Notification is required prior to manufacture or importation for environmental introduction.

- Information will be assessed within prescribed assessment periods. One extension of the assessment period is possible. (Note: the regulations also prescribe a notification period; this period is concurrent with the assessment period.)

- CEPA contains explicit provisions for protecting confidential business information. The degree of protection afforded to information claimed to be confidential will be consistent with the provisions of the Access to Information Act.

- The waiver provisions of CEPA provide flexibility for dealing on a case-by-case basis with specific products where the progression through the stages is either not appropriate or necessary, or for waiving information requirements that may not be applicable for the product. Any request for waivers must be supported and accompanied by a sound scientific rationale.

- A mechanism is proposed for listing specific uses of microorganisms for which notification would not be required.

Wherever possible, Environment Canada and Health and Welfare Canada have adhered to the general principles and approaches being developed worldwide for the regulation of biotechnology products.

CATEGORIES OF NOTIFICATION AND ASSESSMENT PERIODS

Notification for Contained Use of Microorganisms

Microorganisms assessed under this schedule are those not intended for environmental introduction but are used in a contained facility for the production of other products (e.g., chemicals, enzymes) or are used for a contained process. Under the proposed regulations, work in a greenhouse, for example, will be subject to notification as contained use, provided construction and operation of the greenhouse are adequate to be considered contained. Otherwise, the work would require notification as a small-scale field trial.

- **Use in a contained facility for research and development** (Schedule XI).

  The information required in this schedule is basic information about the microorganism, its use, control, and contingency planning. **The assessment period is 20 days.**

  Notification is not required for laboratory research that is conducted in facilities under the **supervision of a Biosafety Committee** and **operating according to Laboratory Biosafety Guidelines**[1] of Health and Welfare Canada and the Medical Research Council of Canada, and in **volumes of 10L or less.** Importation of culture samples (less than 50 mL or 50 mg into such facilities for research is also exempt.

- **Use in a contained facility for purposes other than research and development** (Schedule XII).

  Information required includes detailed identification and description of the characteristics of the organism and data to assess human health effects. The containment procedures must also be described. Note that if the use is not considered to be contained for the product in question, the use will be considered an environmental introduction and environmental data will be required. **The assessment period is 180 days.**

Notification for Environmental Use of Microorganisms

Any application or use of microorganisms outside of a contained facility will be considered to be an environmental introduction. An environmental introduction of microorganisms raises issues that are distinct from those of contained use.

• **Environmental introduction in a small scale field trial** (Schedule XIII).

This is the first step in the assessment of a product intended for use in the environment. The microorganism must be carefully identified and characterized. Requirements for environmental data, human health effects data, and description of the field trial appear in this schedule. The size of a small-scale field trial is defined to be equal to or less than one hectare. For field trials in aquatic systems, the system must be closed (e.g., a pond with no exits). For other uses (e.g., mine shafts, underground aquifers, use near oceans, waste streams) conditions and size of the trials will be determined in consultation with Environment Canada. **The assessment period is 90 days.**

• **Environmental introduction for other than either a small scale field trial or commercial use** (Schedule XIV).

This schedule covers environmental releases involving terrestrial or aquatic areas larger than one hectare, for example large scale field trials. A more complete health effects data package is required. The extent of the environmental data package will be dependent on both the organism and data generated from previous studies, but data from small scale field trials must be provided. **The assessment period is 120 days.**

• **Environmental introduction for commercial use** (Schedule XV).

A full environmental data package which includes data generated from field trials and information on the manufacturing process and manufacturing site is required. The health effects data package is the same as that required in Schedule XIV. **The assessment period is 60 days.**

Note: A product for environmental use which is notified and assessed at each of the three stages described above would be subject to assessment periods totalling 270 days. The information requirements and assessment periods are additive. For example, a product which is to be imported for commercial use, and which has been tested elsewhere, would be subject to the same information requirements and assessment period (270 days) as one that is tested and assessed in a step-wise process.

Exemption of Scheduled Microorganisms

One of the proposals in the draft Regulations is to establish a schedule of organisms or groups of organism which have sufficient history of safe use so as not to require assessment for that use. This schedule would enable exemption from assessment on a use-specific basis and should add an important element of flexibility

to the notification regulations. Criteria for inclusion on the list and candidate organisms are being examined.

Notification for Products of Microorganisms

A major application of biotechnology is the production of various chemicals and polymers by microorganisms. Under CEPA, these substances will be assessed in a manner similar to other chemicals as described in Part I (New Substances other than Biotechnology Products or Polymers) or Part II (Polymers) of the New Substances Notification Regulations. The applicability of data requirements under Parts I and II to biotechnology products is under examination.

GUIDE TO THE INFORMATION REQUIREMENTS

The information requirements specified in the schedules fall into five broad areas; identification and characterization of the organism, intended uses and manufacturing details, environmental information requirements, human health test data and specifics on field trials, where applicable.

The microorganism tested in all sections of the assessment requirements should be identical in form and equivalent in stage of growth, phenotypic and genotypic traits to the product to be used or marketed.

1. Identification of the Microorganism

The identification of the microorganism, the criteria and tests used to determine the identification, other names (synonyms, common names, strain designations), the origin (environmental or other isolate) and strain development and enhancement history should be described. Phenotypic and genotypic characteristics of the microorganism are required.

If the microorganism is the product of genetic modification, the nature and source of introduced nucleic acid, stability and transmissibility of the insertion or change made, and phenotypic effects must be described.

2. Intended uses and manufacturing details

The degree of detail in the information required on the facility and the methods of manufacture is commensurate with the intended use of the product. Information required includes laboratory/manufacture methods, quality control and quality assurance procedures, quantity of manufacture, containment procedures, and waste treatment and disposal procedures.

3. Environmental Information Requirements

Detailed information requirements for environmental effects and fate for environmental introduction are being finalized. It is proposed that information be required in a tiered approach. Environmental effects data could form tier one. After review of the results, data on environmental fate could be requested if concerns are raised that could be answered by fate data. In some cases fate testing may be required depending on the information from the basic biological data. Basic biological data would be required for all submissions.

Basic biological data is required for two purposes: a) to aid in the selection of nontarget substances for effects testing; and b) to provide a basic understanding of the activity of the organism in the environment. Basic biological data includes: information on the habitat and geographical distribution and information on involvement in natural cycles. Other data points include ranges for growth and survival, mode of action (meaning a description of the way in which an organism accomplishes its intended uses), information on the potential for gene transfer and on the stability of any genetic modification.

Environmental effects data include tests on nontarget organisms or substances and changes in interactions and population size of the microorganism. In many cases the target substance will be a chemical. In such cases, information on the pathway of degradation (including the degradation products and intermediate substances) should be reported. In some cases, the product and some intermediates may have to be tested on nontarget substances.

The selection of the nontarget organisms or molecules or chemicals or pathways to be tested will depend on the nature of the organism, the action of the organism in the environment and the intended uses. Consultation with Environment Canada is encouraged for selection of nontarget organisms and other substances to be tested.

The development of environmental fate data will depend in most cases on the results from the environmental effects testing. Where it is determined that there is a significant effect on a nontarget substance, then fate data may be required. Fate testing may indicate that the product will not come in contact with the affected substance (timing of application etc.), thus reducing the risk. Fate data are results from detailed testing on various parts of the life cycle of the microorganism (e.g., survival, multiplication, dispersal) and its interaction with the physical, chemical and biological environment.

The testing for effects and fate should be done at the early stages in simulated environments (so-called micro- or mesocosms) that are appropriate to the test. Further testing could be done during the field trials. In the case of genetically modified organisms, a comparison of the effects and fate to parental characteristics and a review of the perturbations from the characteristics of the parents is encouraged.

Also under discussion in the environmental area are a method to evaluate whether additional information on an organism would be required based on the geographical location of isolation and the nature of the information that should be supplied.

4. Human Health Test Data

Information on the potential for a microorganism to pose a human health hazard can be derived from existing information on the microorganism or its parents and from specific testing. The safety testing methods outlined below are based on requirements developed for microbial pest control agents and provide a generalized scheme for testing a microorganism. It is strongly recommended that applicants consult the Environmental Health Directorate of Health and Welfare Canada before testing to ensure that protocols chosen are acceptable. A combination of in vitro characterisation and animal testing using models appropriate to the organism under study can be considered, but justification for the tests must be provided.

Infectivity/Toxicity The purpose of these tests is to assess the capability of microorganisms to cause disease and tissue injury by invasion of and multiplication within human tissue and to produce toxic effects to humans. Toxicity may be associated with toxin production, metabolic (by)product(s), or cellular components of killed and lysed microorganisms.

An initial test of infectivity should be performed using an unusual route of exposure to maximize the potential for the microorganism to colonise the test animals. The test requires a single study with a single high dose of the microorganism administered intravenously or intraperitoneally depending on the organism. Subsequent tests use common routes of exposure to the microorganism and include acute oral exposure, acute inhalation exposure, and acute dermal exposure.

Tissue Culture (Viruses Only) Testing to determine cytopathic and carcinogenic potential of viruses in mammalian cells must be conducted. Recent guidelines[2] developed by the U.S. EPA offer one set of testing methods and protocols which could be used.

Irritation The microorganisms themselves and/or their metabolites and/or byproducts could potentially act as irritants. Ocular and dermal irritancy studies are required. The protocols for both the dermal and ocular irritation studies in the OECD guidelines[3] are considered adequate for assessing these potentials.

Hypersensitivity and Immunological Effects Microorganisms, metabolites and byproducts, could potentially act as allergens. Hypersensitivity testing is therefore required on the substance. Protocols for any study method should include a positive control group of animals which have been treated with a known sensitizing agent.

Exposure Assessment Methods for quantifying human exposure to microbial products are not fully developed at present. In the

interim, a detailed account of the potential for exposure is required. This should include information on: the use pattern, application equipment and methods, application rates, frequency of application, persons potentially exposed, recommended protective clothing and decontamination procedures.

Recommendation It is recommended that humans in contact with a biological product during testing or manufacture should have a complete medical examination prior to exposure, and at regular intervals thereafter. Special medical attention should be given to potentially immunocompromised individuals.

All studies should follow the principles of Good Laboratory Practice (GLP). The GLP principles of the Organisation for Economic Co-operation and Development (1982),[3] the U.S. Food and Drug Administration[4] (21 CFR 58), and U.S. Environmental Protection Agency[5,6] (40 CFR 160; 40 CFR 792) can serve as guidance.

5. Field Trial Specifics

Field trials are required as one of the stages of development and assessment of a product intended for use in the environment.

Small-scale field trials are defined as being one hectare or less in aquatic, terrestrial or other applications (e.g., oil wells, subterranean mines etc.). In addition, for the aquatic systems and subterranean applications, the sites must be closed systems (i.e., not flowing streams and not connected to sources of ground water).

Information to be supplied for a field trial includes the following.

- The objectives of the trial, including purpose of the research, intended use of the product and the reason that a field trial is required at this point.

- Site details, including the exact location of the site(s), maps, description of the surrounding habitat, size of the trial, and rationale for the selection of the site.

- The type of experimental design and the rationale for using this design, including a plot diagram, any planting or other construction needed, description of the sampling procedures and statistical analyses to be performed.

- Site supervision, including safety procedures, clothing and devices to be used and procedures to restrict public access as necessary.

- Introduction protocols, including a measure of activity of the microorganism to be introduced, formulation and quantity

of the product, the method of introduction of the organism to the trial site and frequency and duration of application or introduction.

- Containment procedures to be used prior to and during the experiment to prevent dissemination.

- Monitoring procedures, including the techniques to be used and the sensitivity, specificity, reliability and practicality of the techniques. Populations of the microorganism and of the general microbial population should be determined before and after application, during the field trial and after the termination of the experiment.

- Termination procedures, including details of how treated material and unused product will be disposed, as well as mechanisms for site decontamination and rehabilitation.

- Mitigation procedures including a description of procedures that could be used to control or eliminate the organism from the environment and conditions that would necessitate such action.

APPENDIX A

Definitions from the *Canadian Environmental Protection Act*

Biotechnology: "the application of science and engineering in the direct or indirect use of living organisms or parts of products of living organisms in their natural or modified forms" (CEPA, Section 3 (1)).

Substance: "any distinguishable kind of organic or inorganic matter, whether animate or inanimate and includes

> **a) any matter that is capable of being dispersed in the environment or of being transformed in the environment in to matter that is capable of being so dispersed or that is capable of causing such transformations in the environment,**
>
> **b) any element or free radical,**
>
> **c) any combination of elements of a particular molecular identity that occurs in nature or as a result of a chemical reaction, and**
>
> **d) complex combinations of different molecules that originate in nature or are the result of chemical reactions but that could not practicably be formed by simply combining individual constituents,**

and except for the purposes of sections 25 to 32, includes

> **e) any mixture that is a combination of substances and does not itself produce a substance that is different from the substances that were combined,**
>
> **f) any manufactured item that is formed into a specific physical shape or design during manufacture and has, for its final use, a function or functions dependent in whole or in part on its shape or design, and**
>
> **g) any animate matter that is, or any complex mixtures of different molecules that are contained in effluents, emissions or wastes that result form any work, undertaking or activity" (CEPA, Section 3.(1)) (Sections 25-32 refer to substances new to Canada)**

Toxic: "a substance is toxic if it is entering or may enter the environment in a quantity or concentration or under conditions

> **a) having or that may have an immediate or long-term harmful effect on the environment;**

b) constituting or that may constitute a danger to the environment on which human life depends; or

c) constituting or that constitute a danger in Canada to human life or health" (CEPA, Section 11).

References

1 Laboratory biosafety guidelines. 1990. Health and Welfare Canada and Medical Research Council of Canada. Ministry of Supply and Services cat. No. MR 21-1/1990

2 Pesticide assessment guidelines, Subdivision M- Microbial and biochemical pest control agents (Part A: Microbial). 1989. Environmental Protection Agency, National Technical Information Service (NTIS), Springfield Va, U.S.A. Publication No. 89-211676

3 Good laboratory practice in the testing of chemicals, final report of the group of experts on good laboratory practice. 1982. No. 42353, Organisation for Economic Cooperation and Development, 2 rue Andre-Pascal, 75775, Paris, France

4 Good laboratory practice regulations; Final rule. 21 CFR 58. 1987. Department of health and human services, Food and Drug Adminstration. Fed. Reg. 52: 33767-33782.

5 Good laboratory practice standards; Final rule; 40 CFR 160. 1983. Environmental Protection Agency, Pesticides Programs. Fed. Reg. 48: 53945-53969.

6 Good laboratory practice standards; Final rule; 40 CFR 792. 1983. Environmental Protection Agency, Toxic Substances Control. Fed. Reg. 48: 53921-53944.

PROPOSED NOTIFICATION REGULATIONS FOR BIOTECHNOLOGY PRODUCTS UNDER THE CANADIAN ENVIRONMENTAL PROTECTION ACT

SEPTEMBER 1990

BIOTECHNOLOGY SECTION
COMMERCIAL CHEMICALS BRANCH
CONSERVATION AND PROTECTION
ENVIRONMENT CANADA

Environment Canada
Conservation and Protection

Environnement Canada
Conservation et Protection

Ottava, Ontario
K1A 0H3

Your file Votre référence

October 18, 1990

Our file Notre référence

RE: **PROPOSED NOTIFICATION REGULATIONS FOR BIOTECHNOLOGY PRODUCTS UNDER THE CANADIAN ENVIRONMENTAL PROTECTION ACT**

Environment Canada and Health and Welfare Canada have been developing notification requirements that will enable assessment of the potential environmental or health effects of biotechnology products. These requirements, to be promulgated in due course as regulations under the new substances provisions of the Canadian Environmental Protection Act (CEPA), will set out information that must be provided prior to the manufacture in or importation into Canada of new biotechnology products. The development of these requirements is now at the stage where input is being solicited from interested parties. A discussion draft of the proposed New Substances Notification Regulations for Biotechnology Products is attached for your review and comment.

The proposed biotechnology regulations define a series of notifications based on the stage of development of the product toward commercial exploitation. Five such development phases have been defined, each of which has prescribed notification and assessment periods, as well as a corresponding Schedule, setting out the information to be submitted. The principles and details of the approach are summarized in the attached background documents.

CEPA defines a new substance as one not on the Domestic Substances List (DSL). The DSL to be published in the Canada Gazette at the end of this year will not contain any biotechnology products. Consequently, all biotechnology products will be considered "new substances" and notifiable under the proposed new substances notification regulations. However, should manufacturers or importers provide satisfactory evidence to substantiate that specific products were in commerce in Canada between January 1, 1984 and December 31, 1986, consideration will be given to including these on the DSL. In addition, certain biotechnology products may have an established safety record when used for specific purposes. Schedule XVI of the draft regulations has been incorporated to provide the mechanisms to exempt such products from notification.

Canada

Environment Canada and Health and Welfare Canada are preparing guidelines to provide additional information and assistance to manufacturers and importers in the preparation and submission of their notifications. These guidelines will elaborate on the statutory information requirements and test procedures. It is anticipated that the guidelines will be available in the Fall.

As part of the consultation process on the proposed biotechnology regulations, it is our intent to convene a workshop in Ottawa early in the new year to bring together representatives of groups having an interest in these regulations. The purpose of this workshop will be to review the written comments received in response to the present request for input. The workshop results will be used in finalizing the draft regulations for formal publication as proposed regulations in the Canada Gazette Part I.

All comments regarding the attached discussion draft regulation should be directed by December 14, 1990, to:

Mr. T. McIntyre
Head, Biotechnology Section
Commercial Chemicals Branch
Environment Canada
14th Floor, Place Vincent Massey
351 St. Joseph Boulevard
Hull, Quebec
K1A 0H3

FAX No. (819) 953-7155

I look forward to your input.

Yours sincerely,

W.M. Zuk

W.M. Zuk
Chief
New Substances Division
Commercial Chemicals Branch

CAPSULE SUMMARY
OF PROPOSED NOTIFICATION REGULATIONS
FOR BIOTECHNOLOGY PRODUCTS
UNDER THE NEW SUBSTANCES PROVISIONS OF CEPA

The *Canadian Environmental Protection Act* (CEPA), passed into law on June 30, 1988, contains provisions for the assessment of environmental and health effects of substances new to Canada. The enclosed draft regulations describe notifications and information that must be provided before a new biotechnology product is manufactured or imported.

GENERAL PROVISIONS

- Products assessed under the proposed Regulations include microorganisms to be used in a variety of applications such as, but not limited to, bioremediation, mineral leaching, degradation of chemicals, mining, waste treatment, waste disposal, chemical production, lignin degradation, microbial enhanced oil recovery, biosensors, and energy production.

- An iterative and staged approach to notification and provision of information is used, based on the stages of development of the product towards commercial exploitation. The corresponding information requirements and assessment periods build on those of previous stages of notification.

- Notification is required prior to manufacture or importation for contained uses beyond the scale of laboratory research.

- Notification is required prior to manufacture or importation for environmental introduction.

- Information will be assessed within prescribed assessment periods.

- CEPA contains explicit provisions for protecting confidential business information.

- The waiver provisions of CEPA provide flexibility for dealing on a case-by-case basis with specific products where the progression through the stages is either not appropriate or necessary, or for waiving information requirements that may not be applicable for the product.

- A mechanism is proposed for listing specific uses of microorganisms for which notification would not be required.

CATEGORIES OF NOTIFICATION AND ASSESSMENT PERIODS

Five stages of development are defined for notification.

For contained use, notification is required:

- prior to research and development beyond laboratory scale (Schedule XI, 20 day assessment period;
- prior to commercial manufacture (Schedule XII, 180 day assessment period).

For environmental introduction, notification is required:

- prior to small-scale field trials (Schedule XIII, 90 day assessment period;
- prior to large scale field trials (Schedule XIV, 120 day assessment period);
- prior to commercial production (Schedule XV, 60 day assessment period).

INFORMATION REQUIREMENTS

Each of the five information schedules specify the applicable information requirements. Categories of information to be submitted include:

- identification and characterization of the microorganisms(s);
- data on environmental fate and effects on nontarget substances in the environment;
- human health safety testing data;
- description of intended uses, manufacturing methods and quality control and quality assurance procedures;
- specifics on field trials including location and procedures to be used during the trial, where applicable.

DISCUSSION DRAFT

PART III

BIOTECHNOLOGY PRODUCTS

Interpretation

12. In this Part,

"biochemical" means a substance, other than a microorganism that is produced by an organism;

"contained facility" means an enclosed building or structure which provides barriers to microorganism release and for which there are operational procedures to prevent microorganism release into the environment;

"environmental introduction" means any deliberate release of a microorganism outside of a contained facility;

"microorganism" means bacteria, mycoplasma, chlamydia, rickettsia, protozoa, fungi, algae, viruses, parts of these microorganisms and any combination thereof;

"small-scale field trial" means an environmental introduction of a microorganism for research and development where such introduction is conducted by qualified personnel and conducted such that dispersal and human exposure will be controlled and involves a terrestrial area not exceeding one hectare or a closed aquatic system not exceeding one hectare.

Information Requirements

13.(1) Any person who manufactures or imports a microorganism that is not specified on the Domestic Substances List shall provide the Minister with the following information:

(a) where the microorganism is a research and development substance and is manufactured or imported for use in a contained facility, the information specified in Schedule XI;

(b) where the microorganism is not a research and development substance and is manufactured or imported for use in a contained facility, the information specified in Schedule XII;

(c) where the microorganism is manufactured or imported for environmental introduction in a small-scale field trial, the information specified in Schedule XIII;

DISCUSSION DRAFT

(d) where the microorganism is manufactured or imported for environmental introduction for purposes other than those mentioned in paragraphs (c) and (e), the information specified in Schedule XIV; or

(e) where the microorganism is manufactured or imported for environmental introduction for commercial use, sale, distribution, test marketing or testing by potential commercial customers or users, the information specified in Schedule XV.

(2) Paragraph (1)(a) does not apply to a microorganism that is a research and development substance and that is

(a) manufactured in a quantity of less than 10 L inclusive of microorganisms and media, for use solely within a contained facility, operated according to Laboratory Biosafety Guidelines developed by the Medical Research Council of Canada and the Laboratory Centre for Disease Control, Health Protection Branch, Health and Welfare Canada 1990, as may be amended from time to time, and under supervision of a biosafety committee; or

(b) imported in a quantity less than 50 mL or 50 g inclusive of microorganisms and media, to a contained facility, operated according to Laboratory Biosafety Guidelines described in paragraph (a) and under supervision of a biosafety committee.

(3) Paragraph (1)(a) does not apply to a microorganism that is manufactured in a contained facility for medical or veterinary diagnoses.

(4) Subsection (1) does not apply to a microorganism listed in Schedule XVI, that is manufactured or imported for use under the conditions specified in that Schedule.

14.(1) Any person who manufactures or imports a biochemical that is not a polymer and is not specified on the Domestic Substances List shall provide the Minister with information specified in section 4 of Part I of these Regulations with the addition of test data on mammalian hypersensitivity, and within the dates prescribed in section 6 of Part I of these Regulations.

(2) Any person who manufactures or imports a biochemical that is not a polymer and is not specified on the Domestic Substances List but is specified on the Non-domestic Substances List shall provide the Minister with information specified in section 5 of Part I of these Regulations, with the addition of test data on mammalian hypersensitivity, and within the dates prescribed in section 6 of Part I of these Regulations.

(3) Any person who manufactures or imports a biochemical that is a polymer and is not specified on the Domestic Substances List shall provide the Minister with information specified in section 8 of Part II, with the addition of test data on mammalian hypersensitivity, and within the dates prescribed in section 10 of Part II.

15. The prescribed date before which

(a) the information referred to in paragraph 13(1)(a) shall be provided, is 20 days before the day the manufacture or importation of the microorganism commences;

(b) the information referred to in paragraph 13(1)(b) shall be provided, is 180 days before the day the manufacture or importation of the microorganism commences;

(c) the information referred to in paragraph 13(1)(c) shall be provided, is 90 days before the day the manufacture or importation of the microorganism commences;

(d) the information referred to in paragraph 13(1)(d) shall be provided, is

(i) 210 days before the day the manufacture or importation of the microorganism commences, or

(ii) 120 days before the day the manufacture or importation of the microorganism commences if information specified in paragraph 13(1)(c) has been previously submitted and the assessment period has expired;

(e) the information referred to in paragraph 13(1)(e) shall be provided, is

(i) 270 days before the day the manufacture or importation of the microorganism commences, or

(ii) 60 days before the day the manufacture or importation of the microorganism commences if information specified in paragraph 13(1)(d) has been previously submitted and the assessment period has expired.

16. The periods within which the Ministers shall assess information are as follows:

(a) for information referred to in paragraph 15(a), a period of 20 days following receipt of the information;

(b) for information referred to in paragraph 15(b), a period of 180 days following receipt of the information;

(c) for information referred to in paragraph 15(c), a period of 90 days following receipt of the information;

(d) for information referred to in subparagraph 15(d)(i), a period of 210 days following receipt of the information;

(e) for information referred to in subparagraph 15(d)(ii), a period of 120 days following receipt of the information;

(f) for information referred to in subparagraph 15(e)(i), a period of 270 days following receipt of the information;

(g) for information referred to in subparagraph 15(e)(ii), a period of 60 days following receipt of the information.

DISCUSSION DRAFT

SCHEDULE XI
(Paragraph 13(1)(a))

Information Requirements in Respect of Biotechnology Products New to Canada

1. For the microorganism and, if applicable, for the parents the following information:

   (a) identification and summary of the basis for the identification,

   (b) source and strain history, and

   (c) name and location of the culture collection where stored.

2. Summary of the means used to genetically modify the microorganism and the genotypic and phenotypic effects of the modifications, if applicable.

3. (1) Intended use or uses of the microorganism, the purpose of manufacture, description of manufacturing methods, manufacturing quantities, containment description and quality control and assurance procedures.

   (2) Estimated number of persons that may become exposed to the microorganism.

   (3) Contingency plans in the event of an accidental release.

4. Report from the Biosafety Committee supervising the work, including identification and affiliation of members of Biosafety Committee, and identification of guidelines applied to the proposed use of the microorganism.

5. All information relevant to environmental and health hazard identification that is in the person's possession.

6. Identification of other government agencies, either foreign or within Canada, that have been notified of the manufacture or importation of the microorganism and the purpose of such notification.

Note

If a request is being made to the Minister to waive the requirement for any of the above items under subsection 26(4) of the Act, sufficient information should be provided to justify the request.

DISCUSSION DRAFT

SCHEDULE XII
(Paragraph 13(1)(b))

Information Requirements in Respect of Biotechnology Products New to Canada

1. For the microorganism and, if applicable, for the parents the following information:

   (a) identification and data validating the identification,

   (b) source and strain history, and

   (c) name and location of the culture collection where stored.

2. Phenotypic, genotypic and ecological characteristics of the microorganism or the parents, including morphology; life cycle; requirements for growth, replication and survival; toxin production; specific resistance factors; known extrachromosomal genetic elements and known mobile genetic elements, if applicable.

3. (1) Detailed description of the genetic modifications to the microorganism, including methodology and generated data that unambiguously substantiate the modifications, and the genetic consequences of the modifications, if applicable.

   (2) Detailed description of the phenotypic modifications resulting from genetic modification including data that unambiguously substantiate the modifications, if applicable.

   (3) Methods to distinguish the modified microorganism including data that substantiate the methods, if applicable.

4. Intended use or uses of the microorganism, the purpose of manufacture, description of manufacturing methods, manufacturing quantities, containment description and quality control and assurance procedures.

5. (1) Test data from acute mammalian infectivity and toxicity tests by pulmonary, oral, dermal, and one of intravenous or intraperitoneal routes.

   (2) Test data from mammalian skin and ocular irritation tests.

   (3) Test data on the potential to elicit hypersensitivity reaction in mammals.

   (4) For viral products, test data from cell culture tests of toxicity, infectivity, and transformation.

DISCUSSION DRAFT

SCHEDULE XII-Continued

(5) Mammalian or human health effects information available in the literature on the microorganism or closely related organisms, or determined during research and development, including hypersensitivity or allergenic reactions.

(6) Estimated number of persons that may become exposed to the microorganism.

(7) For the tests referred to in subitems (1), (2) and (3) the following information:

(a) age, sex, number, species, strain and source of animals tested;

(b) route and conditions of administration; and

(c) dose, concentration and vehicle of test substance.

(8) For the tests referred to in subitem (4), the following information:

(a) identification and source of the cells; and

(b) dose and concentration of the test substance.

(9) Laboratory methods, reference materials, validation procedures, quality control and assurance procedures used in developing test data.

6. All other information and test data relevant to environmental and health hazard identification that is in the person's possession or to which the person ought reasonably to have access.

7. Identification of other government agencies, either foreign or within Canada, that have been notified of the manufacture or importation of the microorganism and the purpose of such notification.

Note

If a request is being made to the Minister to waive the requirement for any of the above items under subsection 26(4) of the Act, sufficient information should be provided to justify the request.

DISCUSSION DRAFT

SCHEDULE XIII
(Paragraph 13(1)(c))

Information Requirements in Respect to Biotechnology Products New to Canada

1. For the microorganism and, if applicable, for the parents the following information:

   (a) identification and data validating the identification,

   (b) source and strain history, and

   (c) name and location of the culture collection where stored.

2. Phenotypic, genotypic and ecological characteristics of the microorganism or of the parents, including morphology; life cycle; requirements for growth, replication and survival; toxin production; specific resistance factors; known extrachromosomal genetic elements and known mobile genetic elements, if applicable.

3. (1) Detailed description of the genetic modifications to the microorganism, including methodology and generated data that unambiguously substantiate the modifications, and the genetic consequences of the modifications, if applicable.

   (2) Detailed description of the phenotypic modifications resulting from genetic modifications including data that unambiguously substantiate the modifications, if applicable.

   (3) Methods to distinguish the modified microorganism including data that substantiate the methods, if applicable.

4. (1) Intended use or uses of the product, means by which use is achieved and target substances.

   (2) Manufacturing methods and quality control and assurance procedures.

5. (1) Field trial objectives, experimental design, site details, site supervision, and microorganism introduction protocols.

   (2) Containment and mitigation procedures.

   (3) Monitoring procedures for the microorganism within and adjacent to the field trial site before, during and after the field trial.

DISCUSSION DRAFT

SCHEDULE XIII-Continued

(4) Mechanisms for trial termination, site decontamination, waste treatment, waste disposal and site rehabilitation.

(5) Record keeping techniques and reporting mechanisms.

6. Test data and information on the biological and ecological properties of the microorganism, including as applicable:

   (a) predicted or natural habitat and geographical distribution;

   (b) mode of action;

   (c) involvement in biological or biogeochemical cycling;

   (d) genetic stability;

   (e) genetic transfer capability; and

   (f) range and optimum for pH, temperature and oxygen requirements for survival and growth.

7. (1) Test data from simulated terresterial, atmospheric, freshwater and estuarine environmental studies that are consistent with the proposed use patterns for the microorganism.

   (2) For the tests referred to in subitem (1) the following environmental effects information, as applicable:

   (a) infectivity, toxicity, pathogenicity, degradation or other modification of structural integrity on target and non-target substances;

   (b) expected routes and life stages or points or pathways of exposure of non-target substances;

   (c) likelihood of changes in range of substances affected;

   (d) changes in competitiveness of the microorganism;

   (e) changes in biological or chemical interactions; and

   (f) changes in population size.

DISCUSSION DRAFT

SCHEDULE XIII-Continued

(3) For the tests referred to in subitem (1) the following environmental fate information, as applicable:

(a) survival;

(b) multiplication;

(c) persistence;

(d) dispersal;

(e) effects on biogeochemical cycling;

(f) response of the microorganism to variation in environmental, chemical and physical conditions; and

(g) interaction with natural microbial populations.

8. (1) Test data from acute mammalian infectivity and toxicity tests by one of intravenous or intraperitoneal routes.

(2) For viral products, test data from cell culture tests of toxicity, infectivity, and transformation.

(3) Mammalian or human health effects information available in the literature on the microorganism or closely related organisms, or determined during research and development, including hypersensitivity or allergenic reactions.

(4) Estimated number of persons that may become exposed to the microorganism.

(5) For tests referred to in subitem (1) the following information:

(a) age, sex, number, species, strain and source of animals tested;

(b) route and conditions of administration; and

(c) dose, concentration and vehicle of the test substance.

DISCUSSION DRAFT

SCHEDULE XIII-Concluded

(6) For the tests referred to in subitem (2) the following information:

(a) identification and source of cells; and

(b) dose and concentration of the test substance.

(7) Laboratory methods, reference materials, quality control and assurance procedures used in developing test data.

9. All other information and test data relevant to environmental and health hazard identification that is in the person's possession or to which the person ought reasonably to have access.

10. Identification of other government agencies, either foreign or within Canada, that have been notified of the manufacture or importation of the microorganism and the purpose of such notification.

Note

If a request is being made to the Minister to waive the requirement for any of the above items under subsection 26(4) of the Act, sufficient information should be provided to justify the request.

DISCUSSION DRAFT

SCHEDULE XIV
(Paragraph 13(1)(d))

Information Requirements in Respect of Biotechnology Products New to Canada

1. For the microorganism and, if applicable, for the parents the following information:

   (a) identification and data validating the identification,

   (b) source and strain history, and

   (c) name and location of the culture collection where stored.

2. Phenotypic, genotypic and ecological characteristics of the microorganism or of the parents, including morphology; life cycle; requirements for growth, replication and survival; toxin production; specific resistance factors; known extrachromosomal genetic elements and known mobile genetic elements, if applicable.

3. (1) Detailed description of the genetic modifications to the microorganism, including methodology and generated data that unambiguously substantiate the modifications, and the genetic consequences of the modifications, if applicable.

   (2) Detailed description of the phenotypic modifications resulting from genetic modification including data that unambiguously substantiate the modifications, if applicable.

   (3) Methods to distinguish the modified microorganism including data that substantiate the methods, if applicable.

4. (1) Intended use or uses of the product, means by which use is achieved and target substance.

   (2) Manufacturing methods and quality control and assurance procedures.

5. (1) Field trial objectives, experimental design, site details, site supervision, and microorganism introduction protocols.

   (2) Containment and mitigation procedures.

DISCUSSION DRAFT

SCHEDULE XIV-Continued

(3) Monitoring procedures for the microorganism within and adjacent to the field trial site before, during and after the field trial.

(4) Mechanisms for trial termination, site decontamination, waste treatment, waste disposal and site rehabilitation.

(5) Record keeping techniques and reporting mechanisms.

6. Test data and information on the biological properties of the microorganism, including as applicable:

(a) predicted or natural habitat and geographical distribution;

(b) mode of action;

(c) involvement in biological or biogeochemical cycling;

(d) genetic stability;

(e) genetic transfer capability; and

(f) range and optimum for pH, temperature and oxygen requirements for survival and growth.

7. (1) Test data from simulated terrestrial, atmospheric, freshwater and estuarine environmental studies and from small-scale field trials that are consistent with the proposed use patterns for the microorganism.

(2) For the tests referred to in subitem (1) the following environmental effects information, as applicable:

(a) infectivity, toxicity, pathogenicity, degradation or other modification of structural integrity on target and non-target substances;

(b) expected routes and life stages or points or pathways of exposure of non-target substances;

(c) likelihood of changes in range of substances affected;

(d) changes in competitiveness of the microorganism;

DISCUSSION DRAFT

SCHEDULE XIV-Continued

(e) changes in biological or chemical interactions; and

(f) changes in population size.

(3) For the tests referred to in subitem (1) the following environmental fate information, as applicable:

(a) survival;

(b) multiplication;

(c) persistence;

(d) dispersal;

(e) effects on biogeochemical cycling;

(f) response of the microorganism to variation in environmental, chemical and physical conditions; and

(g) interaction with natural microbial populations.

8. (1) Test data from acute mammalian infectivity and toxicity tests by pulmonary, oral, dermal, and one of intravenous or intraperitoneal routes.

(2) Test data from mammalian skin and ocular irritation tests.

(3) Test data on potential to elicit hypersensitivity reaction in mammals.

(4) For viral products, test data from cell culture tests of toxicity, infectivity, and transformation.

(5) Mammalian or human health effects information available in the literature on the microorganism or closely related organisms, or determined during research and development, including hypersensitivity or allergenic reactions.

(6) Estimated number of persons that may become exposed to the microorganism.

DISCUSSION DRAFT

SCHEDULE XIV-Concluded

(7) For the tests referred to in subitems (1), (2) and (3) the following information:

(a) age, sex, number, species, strain and source of animals tested;

(b) route and conditions of administration; and

(c) dose, concentration and vehicle of test substance.

(8) For the tests referred to in subitem (4) the following information:

(a) identification and source of cells; and

(b) dose and concentration of the test substance.

(9) Laboratory methods, reference materials, quality control and assurance procedures used in developing test data.

9. All other information and test data relevant to environmental and health hazard identification that is in the person's possession or to which the person ought reasonably to have access.

10. Identification of other government agencies, either foreign or within Canada, that have been notified of the manufacture or importation of the microorganism and the purpose of such notification.

Note

If a request is being made to the Minister to waive the requirement for any of the above items under subsection 26(4) of the Act, sufficient information should be provided to justify the request.

DISCUSSION DRAFT

SCHEDULE XV
(Paragraph 13(1)(e))

Information Requirements in Respect of Biotechnology Products New to Canada

1. For the microorganism and, if applicable, for the parents the following information:

   (a) identification and data validating the identification,

   (b) source and strain history, and

   (c) name and location of the culture collection where stored.

2. Phenotypic, genotypic and ecological characteristics of the microorganism or of the parents, including morphology; life cycle; requirements for growth, replication and survival; toxin production; specific resistance factors; known extrachromosomal genetic elements and known mobile genetic elements, if applicable.

3. (1) Detailed description of the genetic modifications to the microorganism, including methodology and generated data that unambiguously substantiate the modifications, and the genetic consequences of the modifications, if applicable.

   (2) Detailed description of the phenotypic modifications resulting from genetic modification including data that unambiguously substantiate the modifications, if applicable.

   (3) Methods to distinguish the modified microorganism including data that substantiate the methods, if applicable.

4. Intended use or uses of the product, means by which use is achieved and target substance.

5. Test data and information on the biological properties of the microorganism, including as applicable:

   (a) predicted or natural habitat and geographical distribution;

   (b) mode of action;

   (c) involvement in biological or biogeochemical cycling;

DISCUSSION DRAFT

SCHEDULE XV-Continued

(d) genetic stability;

(e) genetic transfer capability; and

(f) range and optimum for pH, temperature and oxygen requirements for survival and growth.

6. (1) Test data from simulated terrestrial, atmospheric, freshwater and estuarine environmental studies and field trials that are consistent with the proposed use patterns for the microorganism.

(2) For the tests referred to in subitem (1) the following environmental effects information, as applicable:

(a) infectivity, toxicity, pathogenicity, degradation or other modification of structural integrity on target and non-target substances;

(b) expected routes and life stages or points or pathways of exposure of non-target substances;

(c) likelihood of changes in range of substances affected;

(d) changes in competitiveness of the microorganism;

(e) changes in biological or chemical interactions; and

(f) changes in population size.

(3) For the tests referred to in subitem (1) the following environmental fate information, as applicable:

(a) survival;

(b) multiplication;

(c) persistence;

(d) dispersal;

(e) effects on biogeochemical cycling;

DISCUSSION DRAFT

SCHEDULE XV-Continued

(f) response of the microorganism to variation in environmental, chemical and physical conditions; and

(g) interaction with natural microbial populations.

7. (1) Test data from acute mammalian infectivity and toxicity tests by pulmonary, oral, dermal, and one of intravenous or intraperitoneal routes.

(2) Test data from mammalian skin and ocular irritation tests.

(3) Test data on potential to elicit hypersensitivity reaction in mammals.

(4) For viral products, test data from cell culture tests of toxicity, infectivity, and transformation.

(5) Mammalian or human health effects information available in the literature on the microorganism or closely related organisms, or determined during research and development, including hypersensitivity or allergenic reactions.

(6) Estimated number of persons that may become exposed to the microorganism.

(7) For the tests referred to in subitems (1), (2) and (3) the following information:

(a) age, sex, number, species, strain and source of animals tested;

(b) route and conditions of administration; and

(c) dose, concentration and vehicle of test substance.

(8) For the tests referred to in subitem (4) the following information:

(a) identification and source of cells; and

(b) dose and concentration of the test substance.

(9) Laboratory methods, reference materials, quality control and assurance procedures used in developing test data.

DISCUSSION DRAFT

SCHEDULE XV-Concluded

8. Quality control and assurance procedures to be used for the commercial product.

9. Site and methods of manufacture, potential sources of release, characteristics of potential release, mechanisms to contain and control release, and treatment and disposal of wastes.

10. All other information and test data relevant to environmental and health hazard identification that is in the person's possession or to which the person ought reasonably to have access.

11. Identification of other government agencies, either foreign or within Canada, that have been notified of the manufacture or importation of the microorganism and the purpose of such notification.

Note

If a request is being made to the Minister to waive the requirement for any of the above items under subsection 26(4) of the Act, sufficient information should be provided to justify the request.

DISCUSSION DRAFT

SCHEDULE XVI
(Subsection 13(4))

Microorganism	Use	Conditions of Use

COPIES OF THE CANADIAN ENVIRONMENTAL PROTECTION ACT CAN BE PURCHASED FROM:

SUPPLY AND SERVICES CANADA
CANADIAN GOVERNMENT PUBLISHING CENTRE
45 SACRE-COEUR
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ABBREVIATIONS

AC	Agriculture Canada
APHIS	Animal and Plant Health Inspection Service (USDA)
BC	Biosafety Committee
BSAC	Biotechnology Science Advisory Committee (EPA)
CBI	Confidential Business Information
CEPA	Canadian Environmental Protection Act
DES	diethylstilbestrol
DNA	deoxyribonucleic acid
DSL	Domestic Substances List
EC	Environment Canada
EIA	Environmental Impact Assessment
EPA	Environmental Protection Agency (U.S.)
EUP	Experimental Use Permit (EPA)
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act (EPA)
FPI	Food Production and Inspection Branch (AC)
GEM	genetically modified organism
GILSP	good industry large-scale practice
HWC	H&WC, Health and Welfare Canada
IBAC	Industrial Biotechnology Association of Canada
ID	identification
IRAP	Industrial Research Assistance Program (NRC)
ISTC	Industry Science and Technology Canada
JOSH	Joint Occupational Safety and Health Committee
MAb	monoclonal antibody
MOU	memorandum of understanding
MRC	Medical Research Council
NOM	naturally occurring microorganism
NRC	National Research Council
OECD	Organisation for Economic Cooperation and Development
PCPA	Pest Control Products Act (AC)
PCR	polymerized chain reaction
PLFA	phospholipid fatty acid analysis
PMN	Premanufacturing Notice (TSCA),
QA/QC	quality assurance, quality control
RAM	risk assessment mechanism
R&D	research and development
RNA	ribonucleic acid
rDNA	recombinant deoxyribonucleic acid
SAP	Science Advisory Committee (FIFRA)
TBI	Toronto Biotechnology Initiative
TSCA	Toxic Substances Control Act (EPA)
UNEP	United Nations Environment Programme
USDA	United States Department of Agriculture

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